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THE ETIOLOGY OF TETANY—METABOLIC AND CLINICAL STUDIES *

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Most authors who have written on the subject of infantile tetany connect the cause with a disturbance of the calcium metabolism, the greater number believing it to be due to a deficiency of calcium in the tissues. Stoeltzner[1] and his co-workers believe there is a stagnation of calcium in the tissues. Cybulski[2] and Schabad[3] are confirmed that the calcium excretion is not regularly increased in tetany; yet the latter finds that on giving cod liver oil and phosphorus, there is a gradual reduction of electrical irritability with simultaneously an increased calcium retention. Schwarz and Bass[4] failed to find any lessening of calcium retention. MacCallum and Voegtlin[5] observed that in parathyroidectomized dogs the injection of calcium and magnesium salts stops all symptoms of tetany and that the injection of sodium and potassium salts has the opposite tendency. In addition to this they found a reduction of the calcium content of the tissues and blood during tetany and increased excretion of calcium in the urine and feces while the tetany is developing. At the same time they found that the ammonia in the blood and urine was also increased. Rosenstern[6] reduced the electrical irritability by giving calcium salts in large amounts per mouth.

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* Read by invitation before the Kent County Medical Society, Grand Rapids, Michigan.

1. Stoeltzner: Jahrb. f. Kinderh., 1906, lxiii, 661; Neurol. Centralbl., 1908, xxvii, 58.
2. Cybulski: Monatschr. f. Kinderh., 1906, v, 409.
3. Schabad: Monatschr. f. Kinderh., 1910, ix, 25.
4. Schwarz and Bass: Am. Jour. Dis. Child., iii, 1, 15.
5. MacCallum and Voegtlin: Jour. Exper. Med., 1909, xi, 118.
6. Rosenstern: Jahrb. f. Kinderh., 1912, lxxii, 154.

Similar use of sodium chlorid resulted in the production of electrical irritability, provided that enough was given to cause a rise in temperature. In addition to these observations he further found that the tetanoid symptoms were reduced on the withdrawal of whey from the food and conversely the symptoms were produced on the addition of it. He did not find sodium and potassium salts as effective in increasing electrical irritability as was whey containing the same amount of sodium and potassium.

Grulee[7] was unable to confirm Rosenstern's findings, except in regard to the experiments with whey. He introduced sodium and calcium salts by injection with negative results. However, the doses used were smaller than those employed by Rosenstern.

Finkelstein[8] says probably some substance in the whey is responsible for the disturbance resulting in tetany. Grulee reports a considerable number of cases of tetany in which a cure was effected by giving a food free from whey curds and barley water, with or without additional carbohydrate.

Zybell[9] in 1913 concluded that experimental results showed no agreement as to the effect on infants suffering from tetany, of long continued feeding of small or large doses of calcium, although occasionally one finds a slight reduction in the electrical irritability in the employment of large doses of this salt. He does not believe in any specific salt therapy.

One of the most important observations from our standpoint has been the observation by Lust[10] in 1913 in which he gave only a clinical report of an infant suffering from severe general edema and typical tetany. The electrical irritability disappeared with the edema. On two successive occasions the edema accompanied by tetany returned and both conditions disappeared as on the first occasion. Of equal interest is Kehrer's[11] report of six cases of tetany of the new-born, in two of which, the mothers suffered from nephritis with edema. Reiss[12] in 1911 stated that he believed that the tetanoid condition depended on the relation between sodium and potassium, on the one hand, and calcium and magnesium on the other. Grulee in further investigations was unable to demonstrate any definite variation in the salts.

Thus it is seen from previous and somewhat extensive observations that there is little uniformity of opinion. By far the greatest number of observations have been devoted towards the detection of the cal-

7. Grulee: Arch. Pediat., 1912, xxix, 24; Am. Jour. Dis. Child., 1913, v, 205.
8. Finkelstein: Lehrbuch der Sauglings Krankheiten, 1909.
9. Zybell: Jahrb. f. Kinderh., 1913, lxxviii, 29.
10. Lust: München. med. Wchnschr., 1913, vi, 93.
11. Kehrer: Jahrb. f. Kinderh., 1913, lxxvii, 624.
12. Reiss: Ztschr. f. Kinderh., 1911, iii, 1.

cium, and no observations either clinical or chemical have proved any definite variations in the balance of the body salts. It might be stated in passing that the trend of opinion goes to show that the parathyroids do not play any definite part in the etiology of this disease, except in assisting generally in the metabolic processes in the body. Many autopsies have shown hemorrhages into the parathyroids, yet the cases clinically have no symptoms of the tetanoid type.

Owing to the observation made by one of us that in several cases of tetany there developed diarrhea, in the course of which the tetanoid group of symptoms spontaneously disappeared, it seemed justifiable to associate the diarrhea with the relief of the tetany. On further investigation it was found that in diarrheal stools the output of sodium and potassium may be eight to ten times that of the normal, while the change in the calcium and magnesium is but slight. Bearing this in mind, it was repeatedly noticed that when the stools of infants suffering from tetany became loose there was an amelioration of the symptoms, depending of course on the fluidity of the movements. Contrary

TABLE 1.—RATIO OF INTAKE TO EXCRETION AND PER CENT. OF INTAKE LOST IN STOOLS

	Normal Stools		Loose Stools		Very Loose Stools	
Fat	12.4	....	23.1	....	40.5	....
Protein	7.7	....	14.9	....	25.2	....
Total ash...	40.0	Urine	46.6	Urine	84.3	Urine
CaO	67.2	Trace	70.2	Trace	79.0	Trace
MgO	56.7	Trace	66.0	Trace	100.0	Trace
P_2O_5	36.9	36.7	41.4	36.0	48.3	41.7
Cl	3.7	79.0	17.7	70.2	52.9	17.0
K_2O	15.4	54.9	37.9	37.9	83.7	26.6
Na_2O	12.3	67.5	37.0	28.2	103.0	5.7

to this, it was also noted that infants afflicted with tetany, either mild or severe, were constipated and that doses of castor oil invariably produced a reduction in the patient's irritability.

At this juncture it is interesting to note what a tremendous output of salts, especially sodium and potassium, takes place in diarrheal stools and for this purpose I have reproduced the table (Table 1) from work done by Courtney and Fales[13] at the Babies' Hospital, New York, Here it will be observed that the output of sodium is a little over eight times the normal while that of the potassium is over five times that of the normal. The calcium and magnesium are influenced only to a much less degree.

It is a general belief, and one which has been most specifically formulated by Reiss,[12] that the calcium and magnesium salts act antagonistically to the sodium and potassium salts, the former tending

13. Courtney and Fales: AM. JOUR. DIS. CHILD., 1915, ix, 213.

to allay nervous irritability, the latter to increase it. In other words, the formula $\frac{Na\ K}{Ca\ Mg}$ would more accurately represent the proposition. When there is a relative increase of calcium and magnesium over sodium and potassium one would expect, if we follow the reasoning on this subject, to have a decreased nervous irritability, while the opposite proposition would also be true.

From what has already been said it will be seen that no observation has yet shown any definite relation between the inorganic salts, on the one hand, and the symptomatology of tetany on the other.

It has been our object to see that if by changing the various food elements, tetany could be produced with a fair degree of certainty, and in addition to this to note if possible any change in the inorganic salts during the onset, height and curing of the condition and what substances were responsible for the ultimate healing.

Our observations have been made on a series of thirty cases of definite tetany and in addition one hundred infants who were thought to be free from tetany were carefully tested, electrically and mechanically, for any evidence of spasmophilia.

METHODS OF OBSERVATION

The clinical methods employed were divided into mechanical and electrical tests. Under the former classification were grouped the various irritability signs, such as Chvostek's, Trousseau's, Schultz, carpopedal spasm, laryngospasm and convulsions. The degree of intensity of each particular sign was denoted by + or + + +, etc. In this manner a fair degree of accuracy was obtained. The electrical tests were made with a galvanic, dry-cell battery equipped with a switch for reversing polarity, a rheostat for controlling the strength of the current and a balanced milliamperemeter measuring from 0.2 to 10 milliamperes.

In every instance the peroneal nerve muscle group was employed, the negative electrode being placed over the upper abdomen and the positive electrode over the peroneal nerve as it winds around the head of the fibula.

The patient to be tested is laid with feet pointing to the right of the observer whose right hand controls the positive electrode placed on the peroneal group. The left hand supports the infant's right foot in such a manner as to detect the slightest twitch occurring in the flexors of the ankle or toes. In this way slight responses are detected which would be imperceptible to the eye. The negative electrode is held in position by an assistant while the observer controls the handle of the rheostat with his elbow. It is essential that all tests should be begun with a current of sufficient strength to produce a good muscular

response, and from this point gradually reduce to a point where the slightest twitch is lost. If the reverse is attempted the lowest contraction point will be invariably passed before response occurs. It is of importance that the reading be made at the point to which the needle on the balanced milliamperemeter swings and not at its highest fluctuation.

The skin resistance varies directly with the amount of subcutaneous fat and reduces rapidly as the operation progresses, the latter fact being apparently due to the congestion developing under the electrodes, thus increasing the skin conductivity. Due allowance should be made for this individual skin resistance so as not unnecessarily to disturb the patient.

It seems to be well supported that electrical irritability may be present when one or all of the symptoms of what is called mechanical irritability are lacking; while, on the other hand, one or more of the latter may be observed without the other mechanical signs or without the electrical reaction.

The most accurate method of estimating the nervous irritability in infants is by the electrical reaction measure by a reliable machine. Escherich in 1909 definitely determined that in infants suffering with spasmophilia KOC is less than 5 ma., while AOC is less than ACC. Speaking more specifically, it requires less than 5 milliamperes of current to produce the cathode opening contraction, while the anode opening contraction is produced by less than is the anode closing contraction. Extensive observations lead us to believe that in the majority of cases of distinct tetany, KOC is not obtained less than 5, but that AOC is always reached before the ACC, which reaction may be spoken of as anodal irritability, and was found to be present in all the cases of the series; in fact in only one instance was KOC noted to be less than 5 ma.

One hundred infants were tested for evidence of mechanical or electrical irritability. Of this group there were only three instances of anodal iritability, in none of which was there a response to a current of less than 2.0 ma. None of this group showed any evidence of mechanical irritability; in other words there was nothing to suggest even a latent tetany. The type of child for control test was chosen at random on admission from a service of sixty beds treating children under 2 years of age.

A diagnosis of tetany was never made when electrical hyperirritability was the only evidence, and further, only variations of 0.2 ma. were considered significant, for below that a personal factor (susceptibility to slight twitch) undoubtedly entered into consideration.

The chemical observations were conducted on a metabolism bed slightly modified from that employed at the Babies' Hospital in New

York. The amount of food taken each day was measured and a proportionate part used for analysis. The urine and feces were collected separately. The specimens dried and ashed by Bunge's method. Sodium and potassium were separated by platinic chlorid and weighed as chlorids. The calcium and magnesium were, according to McCrudden's method, weighed as calcium oxid and magnesium pyrophosphate. In cases in which only the urine was examined the amount of sodium chlorid was estimated according to Volhardt's method.

INCIDENCE OF TETANY

From the accompanying Figure 1 it is seen that tetany occurs almost solely in the fall, winter and spring months; in other words, at a season of the year when there is no tendency towards diarrhea and

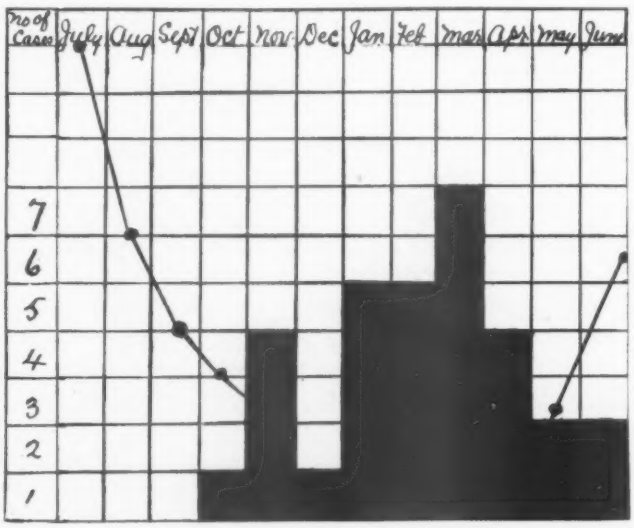

Fig. 1.—Showing monthly incidence of tetany (blocked) in comparison with mortality (curve) from diarrhea.

at which period the general inclination is towards constipation. In contrast to this, one sees no tetany in July and August, during which months the largest number of diarrheal cases occur. This may be explained by the fact that during diarrhea the inorganic salts are constantly eliminated, especially sodium and potassium, as previously noted, and hence the tendency towards irritability, from the storing up of these salts, is removed. On the other hand, during the colder months the infants tend towards constipation; hence elimination and internal combustion is less complete and we have a tendency towards a storing up of sodium and potassium, according to the nature of the food intake. Thus it is seen that the danger of tetany is removed in

the summer months, while the tendency increases at the approach of the cold season.

NATURE OF THE PREVIOUS FEEDING

From Figure 2 it is seen that 78 per cent. of the cases of our series of tetany occurred while being fed on proprietary and cooked foods, while 43 per cent. developed tetany on the former alone. It is worthy of note to see that five cases of the series of tetany occurred while being fed breast milk only. The remaining two cases had been fed various dilutions of pasteurized whole milk mixtures. Whether the milk had been heated beyond the 145 degrees or not it is impossible to state. Figures 3 and 4 depict the percentage of carbohydrate fed to two infants extending over a period of six weeks in one case (Fig. 3) and three months in the other case (Fig. 4); at the expiration of these

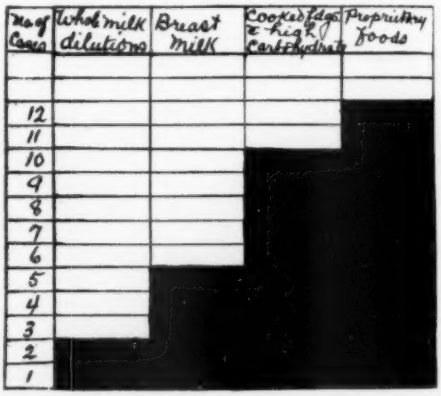

Fig. 2.—Showing the relation of the number of cases of tetany to the previous feedings.

respective periods each infant showed typical electrical and mechanical irritability. The average carbohydrate fed during these periods was 9 per cent., the lowest 4 per cent. and the highest 11 per cent. The fat and protein in each instance were normal for infants of their age. The only other departure from the plain milk feedings was that in each instance the food was cooked for thirty minutes. Both infants gained rapidly in weight and exhibited at the end of the periods of observation a slight degree of craniotabes. We have on record four other such cases fed in identically the same way, and, in each case after a period of a few weeks exhibited, as in these two cases, typical signs of tetany and varying degrees of craniotabes.

It is an established fact that infants fed, over extended periods of time, large percentages of carbohydrates (as is contained in the proprietary foods) develop a water retention and are frequently spoken

of as "water babies." Their resistance is lower than the average child and they succumb rapidly to intercurrent infections and at the onset of diarrhea lose weight in an astonishingly rapid manner. The main increase in weight in carbohydrate fed infants is due chiefly to the fact that they are storing up in their tissues water which is in combination with sodium as sodium chlorid. Whether this ability to store water is due to the fact that the glycogen demands two molecules of water in the tissues, is not yet an established fact.

Another link in the chain of evidence of sodium chlorid retention in the tissues is the fact that when these infants lose their fluid the output of sodium chlorid is eight to ten times the normal. Infants presenting what is known as metabolism edema (due to improper

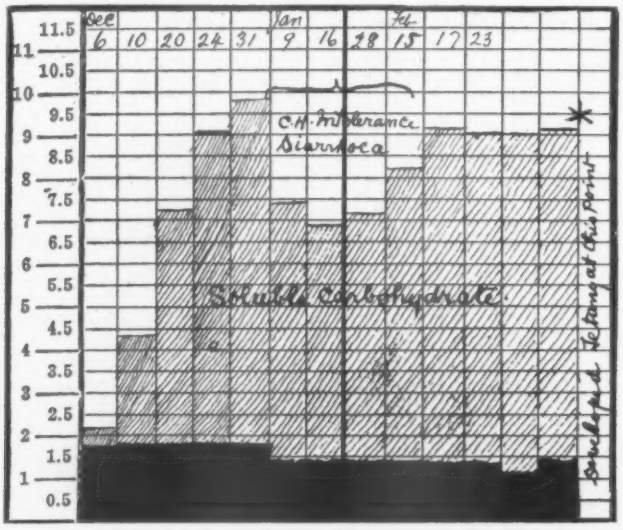

Fig. 3.—T. S. Premature infant. During a six weeks' period, following birth, fed high percentages of carbohydrates and at the end of the period developed tetany. During this period gained 3 pounds and 11 ounces.

feeding) fall into this same class, presenting definite chlorid retention, which rapidly disappears on the subsidence of the edema. In two such cases we have detected definite tetany, the symptoms of which vanished on the disappearance of the edema, coinciding with the increased chlorid output. In support of this evidence might be mentioned Kehrer's[11] observation on five new-born infants developing tetany shortly after birth; the mothers of two of whom had nephritis with edema; and Lust's case of edema and tetany in which the tetanoid symptoms disappeared on the subsidence of the edema and recurred again as the edema reappeared.

It is thus seen that children fed on cooked foods with a high percentage of carbohydrate (as is present in the proprietary foods) show the greatest susceptibility to tetany; in other words, they exhibit a higher water content than normal infants, which water retention is chiefly in the form of sodium chlorid. The sodium and potassium ions, as previously cited, are direct excitants to the nervous tissues. Why it is that infants develop tetany on breast milk is not yet fully determined. It is possible to conceive of the fact that the metabolism of the carbohydrates of the mother's milk is incomplete in these cases, thus favoring a sodium or potassium retention, or on the other hand the total sodium or potassium content of the milk may be abnormally high. We hope to report on this in the near future.

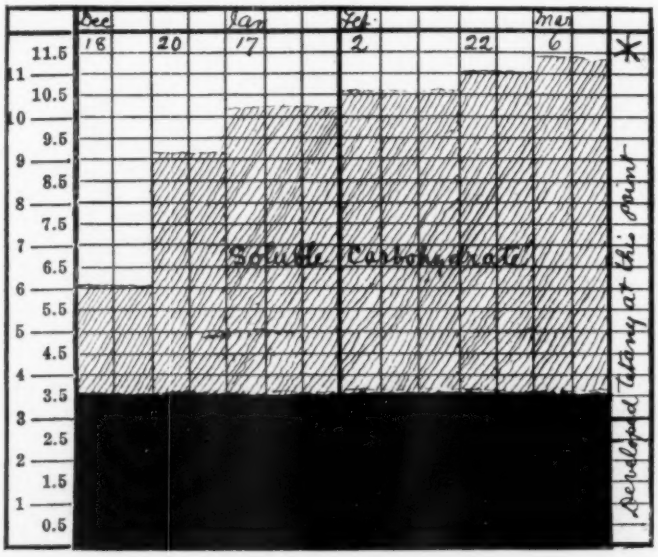

Fig. 4.—Premature infant during a three months' period following birth, fed high percentages of carbohydrates, and at the end of the period developed tetany. During this period gained 2 pounds and 11 ounces.

METABOLISM OBSERVATIONS

The case we have to report in detail presented an excellent opportunity for observation, first, during a period in which the symptoms were severe, and second, during a period of pronounced improvement, ultimately ending in complete cure. A preliminary report of this case with observations and comments has been made in the *Archives of Internal Medicine* by Dr. Almon Fletcher.[14]

14. Fletcher: Arch. Int. Med., 1915, xvi, 382.

REPORT OF CASES

CASE 1.—G. McK., male, aged 13½ months, was admitted Jan. 7, 1915. Had been partly breast fed for nine months, supplemented with Allenbury's food and arrowroot biscuits, while for about one month previous to admission he had had Horlick's malted milk. Throughout, the child was constipated and up to the time of admission the bowel movements were obtained only by means of enemata; the stools being described as small and hard. For the last few weeks previous to his entrance to the hospital he had been cross and irritable. On December 15 he experienced a stiffening of the body accompanied by spasm of the hand and foot, characteristic of tetany. One week later a more severe attack occurred, during which time the child became cyanosed and seemed to struggle for breath. From then on similar convulsions occurred at frequent intervals until the time of admission.

Examination showed only a fairly well developed and nourished child with a moderate amount of subcutaneous tissue of diminished turgor. Enlargement of the epiphyses of the long bones, palpable spleen and a moderate degree of craniotabes were the evidences of rickets.

The child cried continuously, with occasional crowing inspiration. Feet and hands were in the typical position of carpopedal spasm. Chvostek's and Trousseau's signs were strongly positive. Deep tendon reflexes readily elicited, pronounced acetone odor on the breath. The electrical reactions showed distinct anodal irritability KCC = 0.8 ma.; AOC = 1.5 ma.; ACC = 2.2 ma.

We endeavored to approach the same type of feeding that the child had been having previous to admission, in order to eliminate as many extrinsic factors as possible, so, for this reason he was given a mixture containing approximately, fat 2 per cent.; starch 2.5 per cent.; sugar 4 per cent., and protein 1.8 per cent. This combination was obtained by employing evaporated milk, 300 c.c.; barley flour, 45 gm.; lactose, 30 gm., and water, 900 c.c. This was cooked in a double boiler for thirty minutes and water added to make up the loss. He was offered 240 c.c. every four hours for five feedings. A good deal of this was at first refused on account of his extreme irritability.

On January 10 he was put up in a metabolism bed and observed up to January 15. During these five days he had but three constipated movements produced in each instance by castor oil. His irritability consistently increased so that at the end of the period his electrical irritability had increased from KCC 1.0 to 0.4 ma.; AOC 2.0 to 1.0 ma. and ACC 2.5 to 1.8 ma. on the 10th. All his mechanical evidences of irritability showed a corresponding increase. Thus, as well as could be estimated clinically, his tetanoid symptoms had increased considerably, so that on the 15th he might be said to be at the height of the disease. During this period he passed very little urine, although the amount increased toward the end. See Figure 5. During this first stage of observation the child gained 300 gm. in weight.

It had been observed previously that infants fed a high protein diet, such as albumin or protein milk, had an enormous urinary output, sometimes as much as 8 to 10 times the normal. This observation led us to use urea as a diuretic which, being organic in composition, did not interfere with the inorganic estimations such as the other diuretics might have. Since these observations, however, we have found it to be much the superior diuretic for infants.

From January 16 to January 18 the infant was taken out of the observation bed and given 1.0 gm. of urea in the daily quantity of food, to stimulate diuresis, which had already begun. From January 18 to January 22 he was again put up in the observation bed. During this period a striking change occurred (see Fig. 4). The general condition improved, he took more food and seemed to be more contented. The bowels moved without the use of castor oil and seemed more free. The urine increased in quantity from an average of 182 c.c. per diem in the first period to 600 c.c. per diem in the second period.

In other words, a little over three times the amount of urine was excreted during the second period. The electrical irritability decreased from KCC 1.2 ma., AOC 1.4 ma., ACC 3 ma. on January 18 to KCC 2 ma., AOC 2.7 ma., ACC 3 ma., on January 22. The carpopedal spasm entirely disappeared. Trousseau's sign could not be obtained and only a slight Chvostek sign was all that remained of the mechanical irritability. During this period there was a gain of 120 gm. Subsequently the child continued to improve and made a complete recovery.

The daily average estimations for the two periods are represented in Table 2.

From this table it is seen, in Period 1, that there is an abnormal retention of all the salts except magnesium, which, in turn, accompanied a gain in weight due to the retention of fluid. Magnesium is retained in only small amounts. In Period 2 the retained potassium has been cut in half, a daily balance of 0.4464 gm. being reduced to 0.2202 gm. The sodium retention has actually increased 0.002 gm., but the percentage of the intake retained has been reduced from 81.6

TABLE 2.—Salt Intake and Output in Periods 1 and 2

	Intake	Feces	Urine	Loss	Balance
Period 1					
K_2O	0.5460	0.0387	0.0609	0.0996	+ 0.4464
Na_2O	0.1754	0.0194	0.0129	0.0323	+ 0.1431
CaO	0.4686	0.0779	0.0017	0.0796	+ 0.3896
MgO	0.0324	0.00761	0.02155	0.02916	+ 0.0032
Period 2					
K_2O	0.8331	0.0770	0.5359	0.6129	+ 0.2202
Na_2O	0.2706	0.0099	0.1157	0.1256	+ 0.1450
CaO	0.6948	0.2478	0.0081	0.2559	+ 0.4389
MgO	0.1136	0.0279	0.0149	0.0428	+ 0.0706

per cent. to 53.2 per cent. It is of equal interest to note that there has been an increase of 0.049 gm. retention of calcium while the magnesium retention has increased twenty times over that of Period 1.

The striking changes are readily seen in Table 3. Here it is to be observed that both the sodium and potassium retention in percentage of the intake has been reduced, respectively, from 81.6 per cent. and 81 per cent. in the first period to 53.2 per cent. and 26.4 per cent. in the second period. On the other hand the percentage of calcium has decreased from 83.1 per cent. to 63.2 per cent., while there has been a most striking increase in the magnesium balance from 9.8 per cent. in the first period to 62.1 per cent. in the second period.

A mere casual glance at these figures serves to show how calcium estimations alone could not account for either the development or production of tetany. The high magnesium balance is likewise noteworthy in view of its specific action on nerve tissue. This observation

alone in conjunction with those made by Berend[15] and Holt, Courtney and Fales,[16] led us to the employment of subcutaneous injections of a magnesium sulphate solution to control the irritability. So far our results have been most gratifying.

A point of most practical interest is the fact that in Period 2, 88 per cent. of the excretion of sodium and potassium was excreted by the kidneys alone, which excretion occurred simultaneously with an increased flow of urine. In the first period, when the alkalies were retained, the kidneys were remarkably inactive. This observation has been of practical value, for, as will be shown later, the estimation of the sodium chlorid content of the urine alone is of decided diagnostic and prognostic import. In addition it offers a safer method than the production of diarrhea, to rid the body of the offending alkalies.

TABLE 3.—SALT RETENTION, ETC., IN PERIODS 1 AND 2

Period 1			Period 2		
	Retenton in Grams	Percentage of Intake Retained		Retention in Grams	Percentage of Intake Retained
K_2O	+ 0.4464	81.0	K_2O	+ 0.2202	26.4
Na_2O	+ 0.1431	81.6	Na_2O	+ 0.1450	53.2
CaO	+ 0.3896	83.1	CaO	+ 0.4389	63.2
MgO	+ 0.0032	9.8	MgO	+ 0.0706	62.1

The association of suppressed urine and constipation in tetanoid infants is most common; in fact in every one of our cases in which we obtained reliable information, either one or the other and frequently both were prominent symptoms. The association of fluid retention and gastro-intestinal disturbance (constipation) observed in the first period is seen not infrequently in children and the former seems to depend directly on the digestive disturbance, since observation has shown that it can be controlled by changes in the diet and disappears as an improvement in the digestion or general metabolism occurs.

CLINICAL OBSERVATIONS

These observations we have divided into four groups:

1. Showing the effects of diuresis.
2. Showing the effects of purgation.
3. Showing the effects of cod liver oil and phosphorus.
4. Showing the effects of a combination of the above three methods.

15. Berend: Monatschr. f. Kinderh., 1913, xii, 269.
16. Holt, Courtney and Fales: AM. JOUR. DIS. CHILD., 1915, ix, 318.

It must be borne in mind that all the severe cases received one or more doses of magnesium sulphate in order to tide them over the danger period and to enable the instituted treatment to exert some influence in lowering the irritability and thus remove the patient from the danger zone, when the injections were stopped. A detailed report of these injections will be presented at a later date.

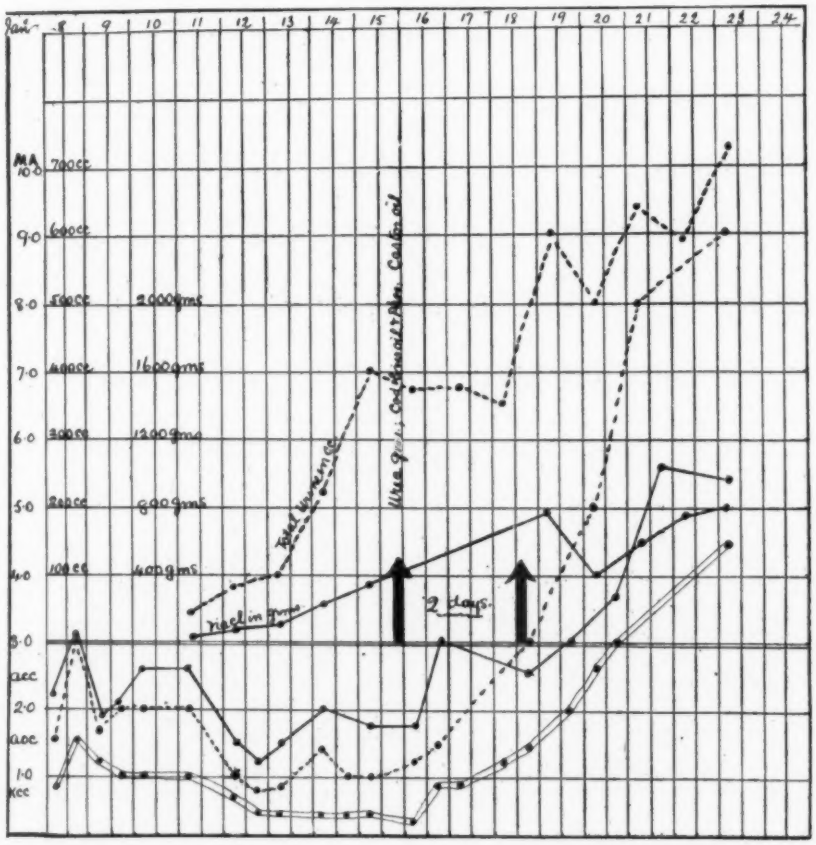

Fig. 5.—Case 1. G. McK. Showing the disappearance of the tetanoid symptoms accompanying the increased urinary output and sodium chlorid excretion.

Group 1: Effect of Diuresis

CASE 1.—G. McK., aged 13 months, admitted January 7. This case has already been referred to under metabolism observations. A brief reference to Figure 5 shows the increasing irritability accompanied by kidney inactivity, and vice versa, at the commencement of increased kidney secretion, which began without a diuretic two days previous to the institution of treatment, but was augmented on the administration of 1 gm. of the organic diuretic urea and 6 c.c. of castor oil. Two days following the commencement of treatment there was complete loss of all irritability which did not again recur. The chlorids had

increased from 0.025 gm. in twenty-four hours to 0.622 gm. at the time of the loss of irritability, a total increase of 96 per cent. over the excretion on admission. As the child improved the chlorid excretion increased until two weeks following cure it was found to be approximately 200 per cent. more than on admission, when the irritability was at its highest. At the time of the administration of urea, cod liver oil and phosphorus treatment was commenced, with the idea according to Schabad's observation, of increasing the calcium retention. It should be noted that observations with the administration of cod liver oil and phosphorus show that there is practically no change in the calcium

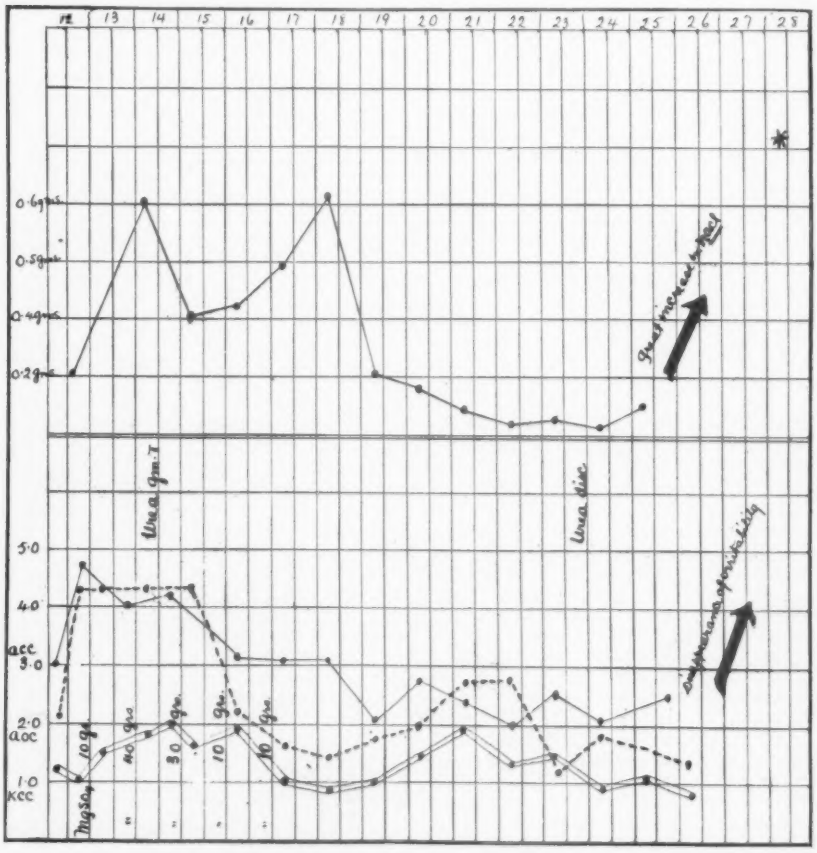

Fig. 6.—Case 2. W. S. Comparing the electrical irritability with the sodium chlorid excretion.

retention till a period of about ten days or two weeks has been reached, so it is obvious that its administration had no effect on the rapid cure of this patient, but undoubtedly aided in the permanent healing which resulted. This plan has been followed more or less in all of our observations.

Case 2.—W. S. (Fig. 6), aged 5 weeks, admitted Jan. 11, 1915, showed pronounced electrical and mechanical irritability. No treatment other than urea was instituted, except subcutaneous injections of magnesium sulphate solution to control the convulsions. Under the exhibition of urea, curiously, the chlorid excretion dropped from 0.235 gm. to 0.075 gm. over a period of nine days; it

was then discontinued and small doses of cod liver oil and phosphorus commenced. In ten days' time the chlorids had reached 0.822 gm. per day, this being coincident with a loss of all irritability as indicated on the chart. This phenomena has been occasionally observed, namely: after the discontinuance of the urea the chlorids increase. We do not think in this instance either that the cod liver oil could have had any such effect, as it was given only in 20 minimum doses, and the response was too rapid. It will be noted on reference to Figure 6 that at the period during low chlorid excretion the irritability was at its height.

Case 3.—J. S. (Fig. 7), aged 15 months, was admitted April 13, 1915, with edema of face and extremities, in addition to which there were pronounced signs of tetany, including extreme electrical irritability. The child was given a plain milk and water mixture and put up in the observation bed. Unaided

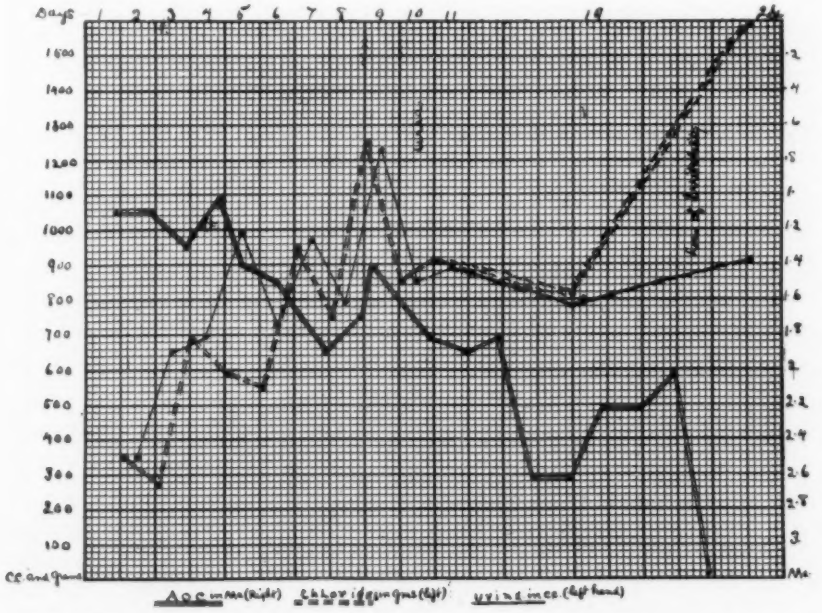

Fig. 7.—Case 3. Comparing the electrical irritability with the sodium chlorid excretion.

a diuresis immediately set in to such an extent that at the end of two weeks he had lost 1,060 gm. in weight, during which time his edema gradually disappeared. The changes that occurred at the same time were, (a) gradual reduction in his irritability, and (b) gradual increase in the sodium chlorid excretion. On admission he was found to be excreting 0.342 gm. in all the first day, and 0.258 gm. the second day; the output gradually rose till eight days following admission when he excreted 1.364 gm. in twenty-four hours or an increase of nearly five times the output at the height of the irritability. In this instance urea had practically no effect in increasing the urinary output as it had already begun and was well established when the diuretic was added. Throughout, the stools averaged one to two a day and were well digested. At the height of the chlorid excretion cod liver oil and phosphorus were given in 3 c.c. doses three times a day which completed the cure twenty-three days following admission. This child then exhibited a tremendous chlorid retention

as manifested by his edema, and later the loss of chlorids. At the height of the edema the tetany was at its worst, the signs disappearing as the chlorids increased.

Group 2: Effect of Purgation

CASE 4.—W. E., aged 6 months, was admitted for convulsions and found to have pronounced mechanical and electrical irritability. During a period of one week the irritability remained practically unchanged with no treatment; at the expiration of this time the child developed a severe diarrhea with seven to eight watery stools a day. In forty-eight hours there was complete absence of all the tetanoid group of symptoms. Many other instances might be cited, only not to such a striking degree. So convinced are we that we do not fear the onset of tetany as long as the bowels are moving freely.

Group 3: Effect of Cod Liver Oil and Phosphorus

To this group belong the cases whose symptoms are not severe and in which it is safe to wait a period of ten days or two weeks before any curative results may be expected.

CASE 5.—F. M., aged 15 months, was admitted April 9, 1915, with fairly pronounced mechanical and electrical tetany. The child was given a diet consisting of whole milk, cereals, beef juice and fruit juice and at the same time 3 c.c. of cod liver oil and phosphorus three times a day. In one week the irritability had slightly diminished and at the end of the following week had entirely disappeared. Throughout, the digestion remained perfect and the stools averaged one a day. The anodal irritability on admission was 1.2 ma., at the end of the first week, 2.8 ma., at end of the second week greater than 3 ma. with no mechanical signs of tetany.

CASE 6.—E. G., aged 8 months, was admitted March 8, 1915, and given a plain milk and water mixture in addition to 1 c.c. of cod liver oil and phosphorus three times a day. The child was suffering from a moderate degree of tetany, the anodal irritability being 2.5 ma. At the end of six days there was a slight increase to 2 ma. The medication was increased to 2 c.c. three times a day. In four more days there was complete loss of all mechanical and electrical irritability.

Group 4: Effect of a Combination of all the Above Three Groups

By this we mean an initial dose of castor oil to clear out the intestinal tract, the administration of urea and cod liver oil and phosphorus. To this group belong the most dangerous and severe type of cases, our idea being primarily to eliminate as much as possible of the stored up sodium and potassium in the feces by purgation, and to continue this elimination by activating the kidneys through the exhibition of urea and then endeavoring to increase the calcium retention through the administration of cod liver oil and phosphorus.

CASE 7.—H. T., aged 6 months, admitted Feb. 2, 1915, with a history of spasms extending over two months, showed pronounced electrical and mechanical irritability, in fact, the child was on the verge of convulsions. Both the mother and nurse volunteered the information that during the past few days the patient had passed very little urine. The infant was immediately given a dose of castor oil to relieve the constipation, urea gm. 1 in the total days' food, which consisted of protein milk, and at the same time cod liver oil and phosphorus 1.5 c.c. three times a day. For the first three days injections of magnesium sulphate were given subcutaneously to control the spasms, which as previously mentioned, were very severe. In three days following admission there was a decided reduction in both mechanical and electrical irritability, and in six days the AOC had risen from 1.2 ma. on admission to 3 ma. There was complete loss of all irritability on the tenth day. The child went on to complete recovery. Although the daily quantity of urine was not measured, a close watch was kept, the nurse in charge reported a great increase in the

urine after the first twenty-four hours, which continued as long as the urea was administered.

CASE 8.—M. S., aged 9½ months, admitted March 2, 1915, suffering from severe convulsions over a period of two weeks, showed on examination severe mechanical and electrical irritability. The same treatment was instituted as in Case 7 of this group. After the first twelve hours there were no more convulsions and on the third day there was a slight reduction in the electrical irritability. On the thirteenth day there was a decided reduction, the AOC having risen from 1.2 ma. on admission to 2.5 ma. Two days later there was complete loss of both mechanical and electrical irritability. The child made a complete recovery.

In these two cases the symptoms had lasted over a period of from two weeks to two months, during which there was ample opportunity for the establishment of a severe salt disturbance, which was evidenced by the convulsions and severe spasms in each case. In both a cure was effected within two weeks from the institution of treatment, and in each case the healing was permanent. All avenues of excretion were utilized and the retention of the sedative salt increased through the administration of cod liver oil and phosphorus.

SUMMARY

An extensive review of the literature reveals the fact that there is little uniformity of opinion as regards the etiology of tetany. Most authors who have written on the subject have associated the disturbance with a lack of calcium in the system and only one author has suggested the possibility of a general salt disturbance, but has cited no definite proof. Metabolism observations on patients suffering from diarrhea reveals the fact that in severe water loss through the bowel the output of sodium and potassium is eight to ten times the normal.

The production of tetany is probably due to the fact that the organism has been storing up fluid in the tissues, which fluid is in combination with sodium and potassium salts. This phenomena is brought about by the feeding of improper foods composed of high carbohydrates which have been subjected to heat. The association of fluid retention and gastro-intestinal disturbances (constipation) is seen not infrequently in children, and the former seems to depend directly on the gastro-intestinal disturbances, since observations have shown that it can be controlled by dietetic changes, and disappears as the digestion improves.

As previously mentioned, carbohydrate and the salts of sodium and potassium are especially liable to induce these changes and may well be reduced when there is any reason to believe that fluids are being retained. Taking away part of the whey from the food, as is sometimes done in the treatment of tetany, is a means of lowering the sodium and potassium intake; the calcium remains in the curd.

Apparently the sodium chlorid estimation in the urine is an index of the irritability, and as the kidney function improves the irritability lessens or disappears. The production of diuresis is a much safer method of elimination than that of purgation. Undoubtedly calcium estimations alone do not account for the nerve irritability in tetany, but would seem to support the hypothesis that the tetany results from a disturbance of the concentration equilibrium of the salts and such salt changes are probably associated with gastro-intestinal disturbances and decreased flow of urine, and, as improvement in the function of these two systems occurs, restoration of the normal salt equilibrium ensues.

CONCLUSIONS

1. Tetany may be produced by high carbohydrate foods which have been subjected to heat up to or over the boiling point.

2. The monthly incidence of tetany is probably due to a disturbance of the gastro-intestinal tract (constipation), decreased internal combustion and the comparative safety from diarrhea in feeding high carbohydrate foods during the cold months.

3. A diagnosis of tetany is suggestive when there is manifest kidney inactivity in constipated infants fed heated foods of high carbohydrate content.

4. As a result of this improper feeding there is produced a disturbance of the body salts. At the height of the disease there is an almost complete retention of sodium and potassium (the irritatting salts) and a great loss of magnesium. As improvement ensues there is an increased flow of urine accompanied by a relief of the constipation, during which the stored up sodium and potassium are rapidly lost.

5. This salt disturbance may be remedied first by purgation, second by diuresis, third by the administration of cod liver oil and phosphorus to build up the calcium content, and fourth by a change of diet.

6. The severe spasms or convulsions may be temporarily relieved by subcutaneous injections of a solution of magnesium sulphate.

We wish to express our thanks to Dr. R. I. Harris for the chlorid estimations, to the nurses, and to Drs. Smith and Binkely of the house staff for their hearty cooperation.

440 Avenue Road—532 Huron Street.

A CONTRIBUTION TO DUCTLESS GLAND THERAPY*

ROYAL STORRS HAYNES, M.D.
NEW YORK

The contribution which I have to make has to do with the action of the pars intermedia of the pituitary gland. These particular activities of the gland, from a therapeutic standpoint, have become apparent through a study of an abnormal child carried on for the past two and a half years by me, and previously by several physicians connected with the dispensary of the Babies' Hospital, including Drs. Kerley and Van Ingen.

The patient was seen first on Sept. 1, 1905, at the age of 3 years and 8 months, when a diagnosis of cretinism was made on a history that she did not walk nor talk and on the presence of coarse, thick hair, an open mouth, a lolling tongue, short thick thighs, a fontanel of 1½ by 1½ inches and a weight of 27½ pounds.

Given thyroid in small doses, she gained rapidly and steadily in weight and height and intelligence. In seven months she was walking and talking and was regarded as very mischievous. At the end of two years' treatment she was bright and intelligent with a closed fontanel and a not greatly protuberant abdomen. Enuresis was noted toward the end of this period.

Shortly after this it was noted that she was not so bright and the dose of thyroid was increased somewhat. She wet the bed a good deal and her skin had a tendency to break out and to be rough. Still she made good progress in weight and height, reaching 45½ inches at 8 years (January, 1910) and 56½ pounds.

At this time she came under the direct charge of an assistant who was an enthusiast who regarded her slowness in mental progress as an evidence that she needed more thyroid, and who proceeded to increase her dose successively from 3 grains a day, the maximum up to then, to 4, 6, 9, 10 and even 15 grains of B. W. & Co. thyroid a day. She had 10 grains a day during the entire year 1912.

This increase of thyroid was not productive of mental improvement, and it did result in an immediate loss in weight and a subsequent development of signs of hyperthyroidism already foreshadowed, perhaps in the enuresis and tendency to rashes, particularly scabs about the nose. She became nervous, irritable, of a poor memory, wet the bed every night and the mentality became even duller.

When she came under my direct care in February, 1913, she was 11 years old, a large child, a little shorter than the average, and a little above average weight. She was dull in school and could not pay attention. She wet the bed every night. She was very nervous and irritable, and had an ugly temper. Her nervousness had reached such a degree as to amount to a positive tremor which had been suspected to be chorea. This prevented her using pen and ink. Her appetite was excessive—she ate all the food that she could lay her hands on—one morning she ate eight rolls for her breakfast.

Her pulse was 120. There was no heart murmur. She weighed 73 pounds and measured in height 53½ inches in stockings.

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* Read at the meeting of the American Pediatric Society, Lakewood, N. J., May, 1915.

It was apparent that she was suffering from too much thyroid, as both the dosage and her symptoms showed. It was decided to omit the drug for a time, instead of merely diminishing the dose. This the mother consented to do, although a little reluctantly, because she had been instructed never to let any one stop giving the child thyroid.

By the next visit we had been rewarded by one dry night and steadier nerves. In a month she had wet only three nights. In six weeks, she was not at all nervous, and did not wet at all. Her weight had increased 10 pounds in this interval.

Because her color was grayish, and because it was feared that some injury might follow too long withdrawal of the thyroid, she received 2½ grains (now known to be plainly too much) for two weeks. She wet the first night it was resumed and in two weeks had lost weight. Thyroid was again withdrawn and kept withdrawn until the fall of 1913.

During the spring and summer of 1913 she improved rapidly, becoming much brighter in school, less irritable, livelier in disposition. She began to pay attention to things she had never noticed before, such as remarks made around her. She learned to read and could no longer be fooled by spelling out words. She began to write with pen and ink, which she could not do before because of tremor.

Her appetite became normal, and while still very good, it was quite easily satisfied. Bed wetting became a lost art.

Along with her remarkable gain in weight, which will be noted on the chart, was the development of the breasts, first noted in June, 1913, and a little hair on the labia. She seemed remarkably normal in every way except that she showed some of her cretinism in her shortness, her lordosis and her prominent abdomen.

In September, 1913, occurred another attack of poor appetite and grayness such as had occurred a month after withdrawal of thyroid. This disappeared promptly with calomel and rhubarb and soda, without thyroid.

However, later in the fall, an attempt was made to improve her condition of slowness, which seemed to be increasing, by giving a preparation of thyroid gland made by Dr. Kendall, then working at St. Luke's Hospital. It was noted that she had become a heavy sleeper, difficult to rouse. She was slow in her motions, which may have had some relation to her greatly increased weight. Her skin was thickened with what looked like the thickness of myxedema, but her color was good and her expression intelligent. Dr. Kendall's preparation "B" was supposed to affect particularly the skin and the intelligence. She had this seventeen days, when the supply ran out and no more could be obtained, as a lot of thyroid obtained from a large pharmaceutical house gave a "B" which was quite inert. This was attributed to bacterial action in improperly kept glands. This drew my attention to the necessity of having absolutely fresh glands and immediate desiccation.

In January, 1914, she began to show definitely the symptoms which we came to call "acromegaly."

During the whole of the preceding six months, at least, it seemed that some other agency had been set at work or released by the withdrawal of the thyroid, because her weight had increased so rapidly and her general bigness, although her height had not.

She now had gained 10 pounds in four months, and almost nothing in height. She looked very chunky; her face was of a heavier cast; she looked older and sullen. Her hands were broad and the fingers blunt. To investigate the possibility of pituitary involvement, her wrist and her head were radiographed and her tolerance for glucose determined.

The sella turcica was enlarged, the antero-posterior diameter being 14 mm.; the depth 9 mm. (Normal adult of same size head A.P. 10.8, D. 7.7.)[1]

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1. Potts: Jour. Am. Med. Assn., Sept. 27, 1913, p. 1188.

The wrist seemed practically normal for her age, which was surprising considering her cretinism.

By mistake, when we came to test her tolerance for glucose, she received 250 gm. instead of 150 gm. Yet she retained it, showing no glucose in the urine.

Acting on the assumption that an increased tolerance for glucose meant a deficient pars intermedia secretion, we concluded, rightly or wrongly, that there was a hyperplasia of the pars anterior causing enlargement of face, hands and feet, and that this might have, by pressure on the pars intermedia itself, or its blood supply, caused its secretion to become deficient. This hypothesis is strengthened by analogy with the pituitary of pregnancy, and by Cushing's statement that an enlarged anterior lobe may exert pressure on the posterior lobe, disturbing its secretion. It was determined to act on this.

A preparation of pars intermedia was obtained in capsule form, each capsule being the equivalent of 150 pounds of live bullock. This preparation has the merit of being dried and made stable within forty-five minutes of the removal of the pituitary from the slaughtered animal. It is mixed with milk sugar and will keep in the cold a year. There is no pars posterior (nervosa) included in the preparation.

Before this was administered, a photograph (Fig. 1) was taken showing the child about March 20, 1914. This shows pretty well her peculiar appearance. She looks more like a little ugly young woman than a child of 12; her face is heavy. The squareness of her figure is accentuated by the prominence of her bust. Her skin was thick and solid, particularly over thighs, buttocks and abdomen. Her complexion had taken on a yellow cast. The skin around her finger nails was scaly, and the skin generally was rather cold and not pleasant to the touch.

She was slow in her motions; a heavy sleeper and hard to waken. She was eager to play, but much slower than other children. She seemed to be learning music, which she loves, and was very apt at learning all the modern dances which she dances well. She was clever with her needle and could trim hats. School work did not go very well. She weighed 106½ pounds and was 54½ inches tall.

After two weeks of capsules, it was noted that the expression was brighter, as if something had lifted from her countenance; her mouth was more closely shut and she said "Hello" briskly when she entered the office. More noticeable was the increased smoothness of her skin and its thinning, which enabled one to pick it up easily, which could not be done previously.

In a month her face had lost its vacant, sullen look. Her skin had improved. She seemed more slow than ever about getting up and about. This may have been due to her increased weight, which had gone to 108 pounds. This increase may have been due to successive attempts to test her tolerance for glucose, which usually resulted in vomiting. Later it was noticed that the weight increased noticeably after these ingestions of glucose—more than the weight of the ingested glucose.

The capsules were continued. By July it had been noticed that in addition to the change in facial expression and skin, there had been a distinct change in the contour of her hands. The fingers became tapering where they had been blunt, distinctly more pleasing to the eye and the touch. Her hips were more slender and shapely; the lower extremities were straighter and the ankles could be brought closer together. The skin was soft and the hair more oily. Her breasts were larger, there was more pubic hair, but no menstruation. Her complexion was pink and white. She had become quick at repartee, but was still a heavy sleeper and routine school work was difficult.

By October she had improved a little in waking. The use of adrenal for two weeks did nothing, while the omission of the capsules of pars intermedia caused a return toward a yellowness and roughness of the skin. She was still slow on initiative, and it was determined to introduce thyroid without the capsules to see its effect.

After three weeks on thyroid gr. 3 to gr. 1, she had lost 3½ pounds; her skin was drier, and her hands a little more blunt, but she seemed keener intellectually, got up of her own accord and had become very talkative.

Pituitary was resumed, 1 capsule and gr. 1 of thyroid, and continued until Feb. 24, 1915, a steady improvement taking place in skin, contour—the hips were very slender and for the first time in a long while she could put on and button an ordinary shoe without setting the buttons over. A photograph was taken then because it was determined to stop the pituitary while continuing the thyroid to see if the pars intermedia was really necessary.

Mentally she had become more alert—she had become an expert dresser, although precipitate in undressing; was fond of reading—such books as the "Five Little Peppers" and the Alger books. She was very inquisitive, and clever enough to be away at dish-washing time. Had become conscious of self—began to care what she had to wear and show some speculative faculty. She said once: "I wonder what I would have been if I hadn't gone to him" (the writer).

Pituitary was omitted until April 13, six weeks, and then a third photograph was taken. While well and retaining her improved figure, there was a certain heaviness of face that had crept into her look and her complexion was yellower, her skin rougher on back of arms, thighs and buttocks. Her fingers were a little blunter. She was slow in her movements.

This experiment was particularly interesting, because when she came to see me on March 16 I had not ordered her to stop pituitary, but contemplated doing so at that visit. When I saw her, I thought she was sick and immediately gave up the idea of doing so. It transpired that the undoubtedly more sullen expression, the yellowness and the thickened face, was due to her mother having stopped the capsules according to what she thought I had directed two weeks before. I felt my judgment sustained by this accident.

Since this time she had had one to three capsules a day and there had been marked and rapid improvement again, in all the characteristics which seem to be affected in her by the pituitary. There has been general improvement in color, clearness, whiteness and smoothness of skin, which feels warm and pleasant to the touch. Even around the nails it is good.

The changes in symmetry are particularly noticeable, as before when taking capsules, the slope of shoulders, slenderness of waist, slenderness of hips, thighs, legs and ankles and straightness of lower extremities. There is less protuberance of abdomen and her lordosis is less marked. The hands seem lower down toward the knees. Her sisters think she has grown taller, but it is only an inch.

To any one who has seen her, she does not appear to be an abnormal child, only a rather heavy, stocky one, very good natured and not sensitive to pain.

Miss Keller, who tested her for intelligence by the Binet-Simon card, remarked on her wonderful complexion.

Her blood pressure now is 100 systolic, diastolic, 70; pulse rate, 72.

She still has a tolerance for 150 gm. glucose.

Her blood sugar (which Dr. Schloss was good enough to determine) is 0.58 per cent.; 3½ hr. p. c.

Her intelligence registers about 9 years, but this is to be qualified by the possibility of an imperfect pedagogic method, inasmuch as she does not attend a special school.

Roentgenogram of sella May 19 shows A.P. 15 mm., D. 9 mm. (this may be distorted).

Roentgenogram of wrist now shows the pisiform.

Photograph, Figure 3, speaks for itself. She has not menstruated.*

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*Menstruation appeared in June, 1915, was profuse, continued a week and was accompanied by a fair amount of pain.

A provocative injection of 0.5 c.c. pituitrin (P., D. & Co.) into the subcutaneous tissue of the right arm following the ingestion of two capsules and 150 gm. glucose produced a faint trace of sugar in the first six hours' specimen following injection.

It seems evident in this case, that, assuming a deficiency of thyroid as evidenced by the condition when first coming for treatment, there is also an affection of the pituitary; that this affection of the pituitary partakes of the nature of a deficiency of the pars intermedia, whether or not one is ready to assume an overgrowth of the pars anterior, and that the exhibition of pars intermedia has improved the condition in unexpected ways.

The questions of whether the pituitary has always been at fault, or whether the overdosing with thyroid has affected it, or the withdrawal of thyroid has simply allowed it to assume an activity, are subjects for pleasurable speculation. I cannot feel certain about it, although as the pituitary symptoms developed, it looked as if they came out from behind a withdrawing curtain of too much thyroid.

It seems evident, also, that the hypothesis on which pituitary medication was started has, as I have indicated, some probability.

The secondary sexual development would seem not to be due to pituitary directly, but to the effect of disturbance of that gland on the interstitial cells of the ovary, known to be closely associated with the pituitary.

There are no neighborhood symptoms and no evidence of tumor.

The effect of thyroid during the past three years seems to have been confined, so to speak, to setting the pace for her initiative, and also in clearing up the scaly skin about the finger nails, although before thyroid was resumed, there was some evidence of benefit in both these conditions under pars intermedia.

The effect of the pars intermedia on the mentality was no less striking than it was unexpected. Perhaps we should say "on the disposition," for the intellectual changes took place to a large degree simply from withdrawal of thyroid, and its present continued low standard may be due somewhat to the child's being in a graded class. However, in liveliness of disposition, sweetness of temper, general interest in things, and a sense of personality, the pars intermedia therapy has seemed to have great effect.

It has been remarkably interesting in following the unfolding of this case to see

1. Symptoms which might rationally have been considered to be due to hypothyroidism clear up with the exhibition of pars intermedia;

2. The remarkable effect which the exhibition of this lobe had on the smoothness, texture, and color of the skin and its warmth;

3. The striking changes in contour of hands, ankles, hips, shoulders, thighs, buttocks, etc., changes which could be made to come or to recede with the giving or taking away of the gland.

I am aware that in the consideration of this case we have come but part of the way, and that it will be necessary to investigate other glands before a final conclusion can be reached. It has taken me a year to determine to my satisfaction the value of and the necessity for the pars intermedia and the essential slowness of the method must be my apology for any incompleteness.

CLINICAL NOTES

F. L., aged 3 years 8 months. Family history negative. No miscarriages. Whooping cough previously. Nursed ten months. Now having general table food.

Sept. 1, 1905: Brought to Dr. Kerley's Clinic at Babies' Hospital Dispensary because baby does not walk or talk. Hair coarse. Thighs thick and short. Mouth open. Tongue out. Diagnosis, cretinism.

September 6: Fontanel 1½ by 1½; weight, 27½ pounds. Having thyroid extract ¼ tablet (? amount) t. i. d. Baby sleeps better.

September 13: Uses eight more words than she did. Is more playful and brighter. Stools normal. Weight, 28½ pounds.

September 20: Increasing in disposition to talk. Plays better, but seems somewhat restless. Thyroid ¼ tablet b. i. d.

September 27: Vocabulary increased by four or five words. Still a little restless. Bowels more regular. Mother thinks child much brighter. Speaks about thirty words. Weight, 28 pounds.

October 4: Had an attack of vomiting and diarrhea; mental condition shows no change. Thyroid gr. ½ b. i. d.

October 18: Vocabulary increasing. Seems brighter. Continue treatment with addition of lard inunctions and salt baths. Weight, 28 pounds.

November 1: Doing well. Weight, 28½ pounds.

November 15: Much brighter. Puts two words together. A little constipated.

November 22: Yesterday used four words together. Weight, 29½ pounds.

December 13: Improving steadily. Talks much more fluently. Fontanel, ½ by ½ inch.

Jan. 17, 1906: Aged 4 years, December 30. Adenoids and tonsils taken out at 3½ years. Is still improving, though more slowly. Words are spoken quickly. Tongue protrudes less. Is brighter and more cheerful. Still constipated. Thyroid to be gr. ½ t. i. d. Weight, 31½ pounds.

March 28: Walks, talks, plays and is very mischievous. Fontanel closed. Tongue in mouth. Mouth still open a little. Legs are straightening. Weight, 32¾ pounds. Height, 35½ inches.

November 23: Tongue is not large. Teeth are poor. Legs are almost straight. Liver and spleen are not felt. Is bright and intelligent. Abdomen is much less prominent. Fontanel closed. Much incontinence. Atropin gr. 1/200 ON OM. Weight, 39 pounds. Height, 38 inches. A. S. S. to internal malleolus, 17⅛ inches, Acromion to tip middle finger, 14 inches. Circumference head, 21⅞ inches. Circumference chest, 21½ inches. Circumference abdomen, 20 inches.

Jan. 16, 1907: Continue treatment. Height, 38 inches.

September 20: Height, 39 inches.

November 20: Much improved in the past three months. Talks better. Is brighter. Teeth very bad. Height, 40 inches. Weight, 48½ pounds. Circumference of head, 22½ inches.

July 11, 1908: Doing fairly well, but mother thinks she is not quite so bright. Increase thyroid from gr. 1½ to 2 a day. Still is constipated.

October 7: Goes to school. Seems to be in very good condition. Height, 42 inches. Circumference of head, 22½ inches.

Jan. 20, 1909: Had measles. Thyroid was stopped for one week. Was very dopey after one week without thyroid. With resumption of thyroid picture cleared up. (A later story tells that child had very severe measles and was practically comatose during it and the physician in attendance regarded the withdrawal of thyroid as concerned in producing her bad condition.)

April 2: Has not seemed as bright lately. Mouth is open all the time. Adenoids are felt. Increase thyroid to gr. 2½ a day.

Jan. 10, 1910: Doing well. Height, 45½ inches. Weight, 56½ pounds.

November 21: Not so bright. Is getting thyroid, gr. 3 a day. Increase to gr. 4. Skin is rough and there are some sores on nose. Used unguent-salicylic acid to arms and body.

Nov. 25, 1910: Skin same. (Change of doctors to an enthusiast.)

May 12, 1911: Memory poor. Poor pupil at school. Still has enuresis. Increased thyroid to gr. 6 a day. Weight, 59¾ pounds.

June 7: Went one night without urinating. Adenoids by palpation. Increase thyroid to gr. 9 a day.

June 28: Scab on nose returns. Urinates frequently, Diminish thyroid to gr. 6 a day.

Sept. 18, 1911: Very nervous. Go to thyroid gr. 4½ a day, with potassium arsenite, gr. 1/100 t. i. d.

Jan. 29, 1912: Enuresis pronounced. Backward at school. Bulimia. Thyroid to be gr. 5 b. i. d.

February 14: Reduce schooling. (About this time according to mother, patient received thyroid gr. 15 a day, B. W. & Co.)

September 18: Nervous. Getting thyroid gr. 5 b. i. d.

Feb. 26, 1913: (Enthusiast resigned.) Now aged 11 years. Large and growing well. She wets the bed, however, every night. Very nervous and irritable; has ugly attacks. Nervousness amounts almost to a tremor. Appetite excessive. Often eats all the food on the table (one morning ate eight rolls). Has been thought to have St. Vitus' dance. Dull in school; cannot pay attention. Pulse 120. No murmur. Weight, 73 pounds. Height, 53½ inches. Stop medicine two weeks.

March 12: Not quite so nervous. Didn't wet last night for first time. Continue. Weight, 77½ pounds.

March 26: Wet two out of fifteen nights (best in years). Not nervous now.

April 9: Is not nervous and does not wet at all. Appetite is fine. Resumed one-half 5 gr. tablet a day. Weight, 83¾ pounds.

April 23: Wet once, the first day of taking thyroid. There seems to be no difference except skin, which assumed a grayish cast at last visit, but now is clear again. Is much brighter in school and much livelier since the thyroid was stopped first. Before this did not pay attention to remarks, but now is keener than the others. Again omit thyroid. Weight, 83¼ pounds. Height, 54 inches.

May 7: Seems very well indeed. Color is all right; just as good without thyroid as with it. Does not think of enuresis any more. Weight, 84¼ pounds.

May 21: Seems O. K. Never thinks of wetting. Now going a whole day to school, which tires her somewhat. Weight, 87 pounds.

June 4: All right in every way. Now eats rationally.

June 18: Body examined. Arms go down 7/15 of distance to knee from anterior superior spine. Shows signs of maturing. Breasts are becoming prominent and there is a little hair on vulva (between labia). Is progressing with her reading and can no longer be fooled by words spelled out. Writes well and with ink, which she could not do formerly because of tremor. Weight, 89½ pounds.

July 16: All right in every way mentally. Appetite quite easily satisfied. Weight, 91 pounds.

August 11: Fine. Continued without thyroid. Weight, 94 pounds.

September 10: Has been ill for four or five days. Has had no appetite and color has been poor. The color resembles the condition in April when thyroid was resumed with the idea that its absence made color poor. Stools and urine not noted. Gave calomel gr. 2 and rhubarb and soda. Weight, 93 pounds.

September 22: Was all right after calomel. Weight, 96½ pounds.

Jan. 27, 1914: Since last note patient has not been seen so frequently, as she was doing well, growing heavier and apparently holding her own mentally. She has, however, been growing very slow in her motions and inclined to lie abed. She is also hard to waken. Her flesh is hard and rather thick. Her color is good and she has an intelligent expression. With the idea that she must need some thyroid, although she seems to do well without it, she has been given for seventeen days capsules of Dr. Kendall's thyroid "B" which is supposed to stimulate the mentality and lessen thickening of the skin. She wet her bed first night of taking this, but this may have been accidental. Her appetite has been better but she is very slow. She has been more talkative in school. She looks very much heavier than when last seen and her facial expression is different. She looks older, rather sullen and heavy—a leonine expression. She skates well but is slow in getting started. She is a splendid sewer and very ingenious at this. Weight, 106 pounds. Height, 54½ inches. Continue without medication. Have roentgenogram of sella turcica and test sugar tolerance.

February: Roentgenogram shows enlarged sella turcica.[2] A. P., 14 mm.; D., 9 mm. Wrist shows practically normal ossification for age. Pisiform nucleus just beginning to show. Test for sugar tolerance. By mistake, patient took 250 gm. glucose instead of 150 gm. Urine examination normal; no sugar. General condition about the same, a large, notably well-developed (secondary sexual characteristics) girl, of pleasant disposition, very chunky and solid, with a stolid expression and a skin which is thickened and of a yellowish cast, not a cretinoid type. Pituitary?

March 19: Child has been getting more peculiar in appearance. Looks like a little ugly young woman rather than a child; face is heavy and sullen; lips rather thick, nose stubby; neighbors say she looks older. This is accentuated by the development of her bust. Skin is thick, particularly over thighs, abdomen and buttocks. Seems to be due to a deposit of subcutaneous fat, for the skin is somewhat nobby like a stretched lipoma but there are no localized fatty tumors. Hands are broad, with stubby fingers and the skin around the finger nails is scaly. Skin over elbows thick and scaly. Occasionally flushes and has a good color. Is very strong. Appetite good, not excessive. Weight, 106½ pounds. Height, 54½ inches.

Disposition is happy, usually, but has sullen fits and ugly fits. She is fond of reading which she has learned to do since February, 1913. She seems to understand what she reads.

Sleeps well; very hard to wake; goes to bed early. Is eager to play but is a little slower than other children. Loves music and seems to be learning this. Dances well—can do all kinds of modern dances and learns these quickly and better than anything else. Is clever with needle and can trim hats. Will not take cold water baths now. (This was thought due to poor circulation of skin, which feels rather cold and unpleasant to the touch.) (Fig. 1.)

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2. Potts: Jour. Am. Med. Assn., Sept. 27, 1913, p. 1188. Average of forty-one normal adult sellae: A. P. 10.8; D. 7.7; maximum 16; D. 10. Children, 12 years, A. P. 7, D. 10; 6 years, A. P. 8, D. 6; 4 years, A. P. 7.5, D. 7; 15 years, A. P. 10.5, D. 7.

Is to have capsules of pars intermedia of pituitary prepared by Mr. Perry.[3]

April 6: Has been taking pituitary capsules for two weeks. Weight, 106 pounds. Height, 54½ inches. Expression is a little brighter. Said "hello" briskly when she came into office. Mouth shuts a little better. More noticeable is the increased smoothness of the skin and "thinning" over the lower thorax. Still doesn't wake up unless shaken. A slow dresser. Continue.

April 22: Face has lost vacant, indifferent leonine look. Expression brighter. Still awfully sleepy in morning. Lazy; does not want to walk. (Due to weight?) Appetite O. K. Bowels more or less constipated. Skin has improved. Skates well when she gets started. Seems worse than ever about coming when called. Weight, 108 pounds. Urine not so abundant. Attempt to test sugar tolerance difficult because of tendency to vomit; 150 gm. glucose not followed by any glucosuria. (May weight be due to several attempts with glucose?)

May 25: Had indigestion at time of trying tolerance. Vomited glucose five times. Has been taking capsules for two months. Out of them last few days. Expression shows improvement. Skin shows improvement. Is just as

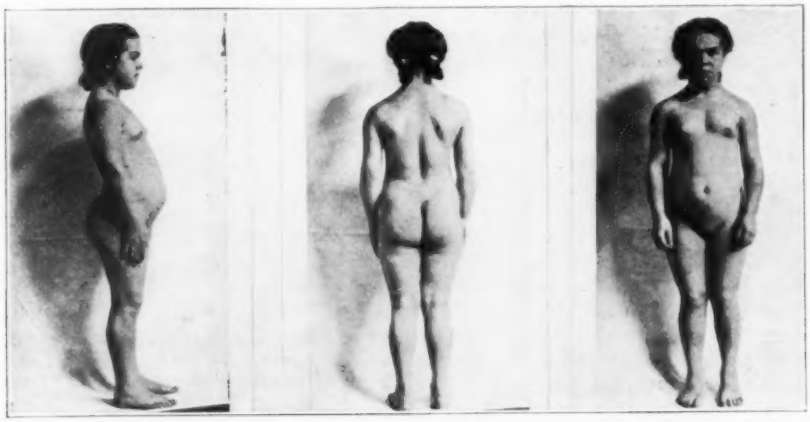

Fig. 1 (Series 1).—Author's patient, taken March, 1914.

heavy a sleeper. Begins to take her own part against others and "scraps." In play has not initiated anything; still slow. School work still not good, and she talks a good deal and gets poor deportment marks. Breasts continue to enlarge and the hair on vulva to become longer and thicker. No menstruation. Appetite is not so good; just over indigestion; bowels more or less consti-

3. *Preparation of Pars Intermedia Capsules.*—The material is collected at the abattoir on the morning of killing. The fresh pituitary gland of the bullock is taken to the laboratory within fifteen to thirty minutes of the killing. The pars intermedia is dissected off and dried at once, the drying being completed within forty-five minutes. It is mixed with milk-sugar and the finished product in capsules may be ready within one and a half hours after killing. The pars posterior is not included. Each capsule represents as nearly as possible, the pars intermedia of 150 pounds of live bullock. These capsules will keep in the cold for a year. The great essential is promptness in drying after removal of gland, as bacterial action may destroy the active principles in a very short time. Any preparation made from glands kept in cold storage or as much as twenty-four hours old will probably be much less efficient if not inert. Dr. Kendall's preparation could not be continued because he ran out of his first lot, and a second supply made from another lot of thyroid—somewhat old—was inert.

pated; gets medicine every Friday night. Blood examination (figures lost) showed nothing abnormal in differential. Specimen of urine one week after stopping capsules showed no glucosuria after 150 gm. glucose. She stands up straighter and has grown ⅝ inch. Weight, 105 pounds. Height, 55¼ inches.

Two observers independently have noticed a change in her hands, which is apparent today. Hand has a less heavy, blunt look. Fingers are more tapering. Hand is distinctly more pleasing to the eye and skin is softer. Nothing detected about feet. There is a change in the lower extremities; legs are more approximated; not so great a deviation; ankles can be more nearly brought together. Complexion not so yellow, in fact almost pink and white. Disposition pleasanter; not sulky; takes and gives jokes. Resume capsules.

July 6: Tanned. Appetite good but not too good. More or less constipation. Sleeps well; waked a little more easily. Plays actively; cannot yet keep up with other children, but does not mind. Initiates games and roller skates faster. Laughs easily and is very quick at repartee, which is a great change. Not much change in school work. (Goes to a parochial school where the pedagogic method may not be adapted to her.) Skin is nice and soft. Hips are more slender. Hands better shape. Hair more oily. Breasts larger. Hair on pubes. Legs are hard as iron. Abdomen still pendulous and lordosis noticeable. Bicuspids said to be abnormal. Teeth are generally good.

October 2: Has not had any pituitary for two weeks. Took it all summer during my absence, working it up to four capsules a day once when she had a month of rather bad temper. Is talkative and inattentive in school. Has been promoted but finds all day hard. Skin is still good, but face is a little heavy. Wakes much more easily. Breasts well developed. Hair has increased. Blood pressure, systolic, 90; diastolic, 50; pulse rate, 84. Weight, 106¼ pounds. To try what effect, if any, adrenal has. Tabloid adrenal gr. 5 O. D.

October 23: Skin yellow, pimply. Not so well. Stop adrenal. Give thyroid B. W. Co. gr. 3 a day. Sphygmomanometer out of order.

November 7: Been on thyroid gr. 3 a day. Height, 55½ inches. Weight, 103 pounds. Is brighter and quicker. Skin is drier then when taking pituitary. Look is keener and more thoughtful; not so indifferent and smily. Hands are less tapering than they were last June.

November 14: Look is more straightforward. Gets up of her own accord. Sews a lot and has considerable initiative. Likes to read a lot and to be alone. Very talkative since taking thyroid. Arithmetic her *bête noir*. To have gr. 1 thyroid b. i. d., and one pituitary capsule.

November 28: First five nights on which she took two medicines she wet four times (first in about a year). Mother thinks she has improved. Gets up better. Not brighter in school. Still talkative. Wants to go out more. Pulse, 100. Weight, 103 pounds. Height, 55 inches. Skin again soft and smooth. Continue.

December 12: Better than she has ever been. Brighter. Color better. Expression is best yet; intelligent and thoughtful. Plays actively; is not now always the last one. But is inattentive in school. No wetting. Weight, 102¾ pounds. Skin has improved; even on belly it is softer, smoother and thinner. Hands taper. Hair on pubes same. General figure is slenderer.

December 18: Has wet five out of six nights. Not so good tempered and possibly not so bright. Color not so good this week. Pulse, 84. Blood pressure, 90-50. Weight, 101½ pounds. Stop thyroid one week. Continue pituitary. Glucose, 100 gm.; had tolerance for this.

December 29: Tomorrow aged 13 years. Has had a cold. Color was not quite so good a week ago; better now. Does not seem quite so fine as when she got thyroid gr. 2 and one capsule, but weight is better and has not wet bed.

Has become very inquisitive in the last couple of weeks and notices things she would never notice before. Appreciates things better. Initiative still

increases. Does not want to be alone so much. Plays well. Is more self-conscious than formerly. Begins to care what she has to wear. Has more individuality, which is shown also in expression of face; is more thoughtful and more aware of being an individual. She has always been sympathetic. Her movements are very decently active and alert. She dresses herself quite expertly and is precipitate in undressing. Is very strong physically. No menstruation. To have gr. ½ B. W. thyroid a day. One capsule pituitary. Weight, 102½ pounds. Height, 55½ inches.

Jan. 14, 1915: For the first few days on gr. ½ thyroid was ugly and general color was not so good. Mental condition about the same; is a little slow in getting ready for school. Appetite good; eats plenty. Fingers are quite normal. Hand is noticeably of nice contour. For the first time ankles can go into an ordinary shoe without changing buttons. Weight, 104¾ pounds. Height, 55½ inches.

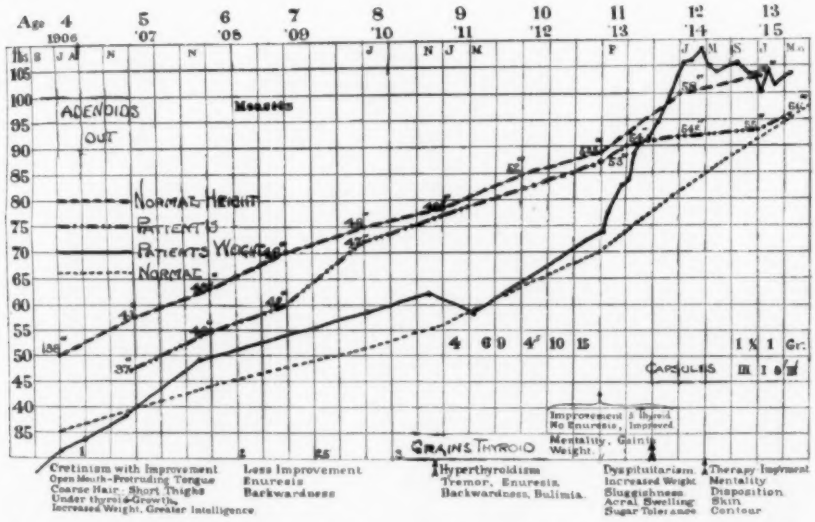

Fig. 2.—Chart showing patient's progress in weight and height with thyroid, with excessive thyroid, without thyroid, with pituitary alone, and with pituitary and thyroid. Also indications as to change in mental characteristics.

January 29: Does not look so well as last time. Nails are again scaly. Weight, 103½ pounds. Give gr. 1 thyroid a day and one capsule pars intermedia. Photograph by Dr. Kilmer (Series 2).

February 24: There is a noticeable change in figure toward slenderness and normal contour. Said to have "a shapely figure." Skin is very soft and smooth except a little at finger tips. Face has a good expression of quiet intelligence. Pubic hair is quite abundant. Breasts large. Lordosis not so noticeable. No wetting. Bowels constipated (to have cascara).

Mathematics still a stumbling block; is much better at dressing; gets up more willingly; plays well and keeps up with the others at play. Still inattentive at school. Nice whistler and dancer. Very fond of reading such books as "Five Little Peppers" and the Alger books. Very full of questions. Clever enough to be always away at dish-washing time. Shows some imagination. Said, "I wonder what I would have been like if I hadn't been going to him" (Dr. Haynes). Pulse, 80. Head, 22½ inches. Chest, 28½ inches. Trochanters, 34. Weight, 103 pounds. Height, 55½ inches. Here planned to stop pituitary

to see if it really was necessary and had done what it had been thought to do. Not ordered stopped.

March 16: When she came into the office she seemed sick in some way which was determined to be a more sluggish expression and a yellower color and slightly swollen face. Determined not to stop pituitary yet, when mother told me that she had understood me to say stop it and had done so two weeks before. Face distinctly heavier; skin rougher on hands, arms, back, and buttocks. Face pimply. Anterior surface of body about same. Curvature of back more like first picture. Has been sullen and irritable. Continue without pars intermedia capsules.

April 1: Still without pars intermedia. Skin roughened in spots, particularly back of arms, thighs and buttocks. Laugh seems less intelligent; said to talk sillier things. Hair on pubes increased. Breasts larger and patient is aware of them. Apropos of their prominence said, "I know I am going to have children when I grow up." No axillary hair. Hands blunter.

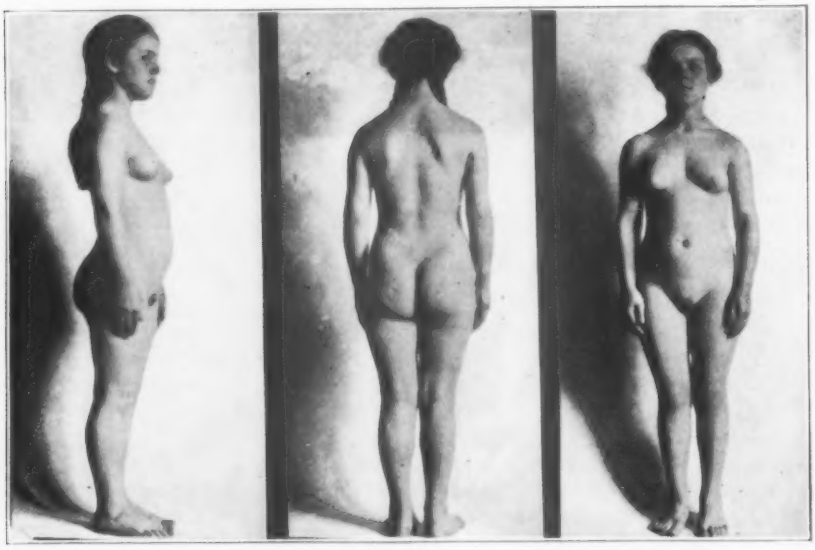

Fig. 3 (Series) 4).—Taken May, 1915. Had been receiving one to three capsules a day, and 1 gr. B. W. Co. thyroid since April 13.

April 12: Still without pituitary. Having thyroid, gr. ½ b. i. d. Is cross and ugly. Face heavier. Looks heavier in motions and figure is less symmetrical; rather clumsy. (Series 3.) To have 150 gm. glucose. Tolerance. Resume pars intermedia capsules after test.

May 5: Has had two capsules of pars intermedia a day and 1 grain of thyroid.

There is a marked improvement in symmetry since last visit. Skin is finer and noticeably whiter. Skin pretty good around nails; elbows almost smooth again; hands again taper. Breasts larger; more hair on genitals. Hair generally more oily again. Expression more intelligent; happier, gentler, sweeter. Doing better in school. Moves more quickly, both general motions and motions of eyes. A few pimples remain. Try three capsules a day.

May 14: General improvement in color, clearness of face and nails, whiteness and smoothness of skin, which feels warmer and very pleasant to touch. The changes in symmetry are particularly noticeable as before when taking

capsules, in slope of shoulders, slenderness of waist, slenderness of hips, thighs and legs and ankles, and straightness of lower extremities. Less protrusion of abdomen and lordosis less marked. Hands seem lower down than formerly, which may be due to slope of shoulders. Neighbors who have followed case see marked improvement and one not familiar with case would see simply rather a heavy, stocky child, but not an abnormal one. Blood pressure, 100-70; pulse, 72. Weight, 103½ pounds. Height, 56 inches.

May 18: Has tolerance to 150 gm glucose.

May 19: Blood sugar (Dr. O. M. Schloss), 0.058 per cent.; just below normal, 3½ hr. p. c. Binet-Simon test for intelligence, 9 years, with recommendation for special training, with emphasis on teaching from concrete to abstract. (Miss Keller exclaimed on patient's wonderful complexion, its fairness and smoothness.)

Roentgenogram of sella, 15 mm. A. P.; 9 mm. D. (This photograph probably was a distorted view, as it was not taken with especial care to avoid distortion.)

Roentgenogram of wrist normal for age; pisiform showing.

May 22: Administration of two capsules at 12:30 p. m. Administration of 150 gm. glucose at 1 p. m. Injection of 0.5 c.c. Parke Davis "pituitrin" into subcutaneous tissue of right arm.

Blood pressure before taking capsules, systolic, 107; diastolic, 75; pulse, 72. After injection, systolic, 105; diastolic, 70; pulse, 72.

Urine first six hours, 1.036; faint trace of sugar; last eighteen hours, 1.030; no or very faintest trace.

Height and weight of other members of her family: Sister, aged 16 years, height 67 inches; weight 132 pounds; father, height 74 inches, weight 214 pounds; sister, aged 19 years, height 67 inches, weight 145 pounds.

THE SPINAL FLUID IN POLIOMYELITIS AND ITS DIFFERENTIATION FROM FLUIDS OF OTHER INFECTIONS *

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A review of the literature reveals comparatively few extensive studies of the cerebrospinal fluid in acute poliomyelitis. This fact is due perhaps to the lack of opportunities for such studies, or to the failure to appreciate the value of the changes in such fluids.

Wickman[1] in his exhaustive monograph on poliomyelitis pays only scant attention to the subject of the fluid in this disease. Römer and Joseph,[2] too, slight the value of examination of fluids in their discussion of diagnosis. They have been particularly interested in the attempt to demonstrate specific substances in the fluid and serum by complement fixation. In this attempt they have failed, as also have Wollstein[3] and Gay and Lucas.[4]

Plaüt,[5] Rehm and Schottmüller devote a page to the cerebrospinal fluid of poliomyelitis in their book on cerebrospinal fluids. They say that cerebrospinal fluids in poliomyelitis contain no globulin and that the average cell count is 15 per cubic millimeter.

Forbes[6] reports the examination of 33 cerebrospinal fluids of which 8 were bloody, due no doubt to accident in technic. Of these, 24 contained albumin in varying amounts. Six showed a heavy precipitate. Cytologic examination showed increase of cells in all but 6, twenty-one fluids having only a slight excess. Very few polymorphonuclears were found, small mononuclears being the most common type. He found that the cell reaction was in direct proportion to the albumin content. All of these cerebrospinal fluids reduced Fehling's solution normally.

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* Read before the Joint Meeting of Brooklyn Pediatric and Neurologic Societies, May 26, 1915.

1. Wickman, Ivan: Jour. Nerv. and Ment. Dis., Monograph 16, 1913.
2. Römer and Joseph: München. med. Wchnschr., 1910, vii, 568.
3. Wollstein, Martha: Jour. Exper. Med., 1908, p. 476.
4. Gay and Lucas: Arch. Int. Med., 1910, vi, 330.
5. Plaüt, Rehm and Schottmüller: Leitfaden zur Untersuchung der Zerebrospinal flussigkeit, Gustav Fischer, 1913.
6. Forbes, J. G.: Lancet, London, Nov. 18, 1911.

Morse[7] reported thirteen examinations of cerebrospinal fluids in seven cases and found pathologic changes in all. All fluids were clear, with one exception, and this was opalescent. The small mononuclear cell was the predominating type of cell. He does not find any aid from the examination of the spinal fluid in differentiating poliomyelitis in preparalytic or abortive form from tuberculous meningitis.

Gay and Lucas[4] have made an interesting cytologic study of spinal fluid from 6 cases of monkey poliomyelitis, noting changes in all stages of the disease. In the incubation period the cells were increased from 100 to 300 per cubic millimeter. They were largely of the large mononuclear type with some polymorphonuclears. In the prodromal period the count went up to 1,000 per cubic millimeter. In this stage polymorphonuclears were increased, in some cases, up to 60 per cent. In the early acute stage, the increase of cells was still very great but the lymphocytes were the predominating cells. At the end of a week or ten days, there were very few cells present, mostly large mononuclears and a few polymorphonuclears. They also report on thirteen spinal fluids from 4 human cases, all of which showed the large mononuclear cell present in varying numbers.

Probably the best and most comprehensive study of the cerebrospinal fluid in poliomyelitis in the American literature is that of Peabody, Draper and Dochez.[8] They tabulate and analyze the findings in 233 spinal fluids from 69 patients. The conditions of their study were such as to permit the following up of the changes in the fluid from week to week, and they have compiled the results admirably. All but two of the cases presented abnormal changes either in cell content or chemical constituents, most frequently in both. The predominating type of cell was the small mononuclear. In some cases, early in the disease, polymorphonuclears were present up to 80 to 90 per cent. of the total count. Mention is made of large phagocytic cells, containing vacuoles and broken down cells as being present in some cases. A grouping of the spinal fluids into two distinct types is made, the one with a high cell count and a low globulin content; the other, with a comparatively low cell count and a high globulin content. The former is found most frequently in the early part, and the latter in the later part of the acute stage.

Four preparalytic and two abortive cases are included in this report and are of particular interest inasmuch as these are the types of cases that present the greatest difficulty in diagnosis. Two of these patients that developed paralyses showed a high cell count. Three

7. Morse, J. L.: Arch. Pediat., 1911, xxviii, No. 3.

8. Peabody, Draper and Dochez: Monograph 4, Jour. Exper. Med., June 24, 1912.

others showed only a moderate increase in cells. Of these two developed paralyses and one was an abortive case. The remaining one, an abortive case, presented a normal spinal fluid on first examination, but the cells were found increased in later specimens. They urge that though the cerebrospinal fluid of poliomyelitis does not present a specific picture, it is of the utmost value as an aid, particularly when considered in conjunction with the clinical aspects of the case, in clearing up the diagnosis in the abortive type and in the preparalytic stage.

The material for the present report was taken from the records of the meningitis department of the New York City Board of Health and covers a period of four years. It consists of the examination of forty-seven cerebrospinal fluids from twenty-nine patients, twenty-seven of which were seen by members of the meningitis staff in consultation with physicians throughout the city. Comparatively few of these patients were seen more than once, and we were, therefore, unable to observe the changes in the various stages of the disease that the Rockefeller Institute workers so ably described. However, this work compensated in the great interest produced by the necessity of arriving at a correct diagnosis through the examination of the spinal fluids, as the majority of the cases were of the meningitic and encephalitic varieties.

Of the 47 fluids, 2 were contaminated by blood and 2 were otherwise unreliable. Of the remaining 43, 10 were from cases diagnosed as myelitis, 21 from encephalitic, 6 from myeloencephalitic, and 6 from abortive cases. Of the 10 myelitic cases, 5 fluids were examined in the preparalytic stage and 5 in the postparalytic stage. Of the 21 encephalitic fluids, 17 were from patients without paralysis, many of which properly belong to the meningitic type, and 4 were from cases with involvement of the cranial nerves. The 6 fluids of the myeloencephalitic group were obtained from cases that presented involvement of both the cranial nerve nuclei and anterior horn cells. The abortive cases showed no signs of paralysis. We feel quite secure in the diagnosis of the cases not showing paralysis, by the clinical characters and outcome of the cases, and in fatal cases, by the negative results after inoculation into two guinea-pigs.

Of the 43 fluids examined, 28 were obtained in the first week of the disease; 8 in the second week, 5 in the third week and 2 in the fourth week.

The routine of our examination consists of a description of the amount and gross appearance of the fluid; an estimation of the cell contents, as to whether there is no increase, a moderate increase or a great increase. This was accomplished by centrifuging 10 to 15 c.c.

of the fluid at high speed for one-half hour and examining three or four platinum loopfuls of the sediment spread on a slide and stained; a rough differential count of the types of cells present; also making note of unusual types of cells. The fluid is then examined bacteriologically on smear and in culture. If smear is negative for organisms, 5 to 10 c.c. of the fluid is inoculated into each of two guinea-pigs. The chemical examination consists of the estimation of the albumin and globulin content and the reduction of Fehling's solution. The albumin and globulin content is graded in + signs, beginning with ± and ascending to 4 +, depending on quantity of precipitate. A ± is considered as that very faint haze present in normal fluids, and 4 +, the maximum, represents the very heavy precipitate obtained most commonly in purulent fluids. The reduction of Fehling's solution is graded, negative when there is no red precipitate at the end of 15 minutes; 1 ± when there is a slight precipitate at the end of that time; 2 + when there is moderate precipitate and 3 +, the maximum, when there is an immediate and heavy reduction. This latter reaction is encountered in practically all normal fluids.

The quantity of fluid withdrawn varied from 5 to 100 c.c. We usually withdraw as much as will readily come, minimizing the suddenness of withdrawal as much as possible. Practically all the fluids that are much in excess of normal come out under varying degrees of pressure, though no direct method of measuring same was used. Thirty-eight fluids were clear; one slightly turbid; one opalescent; three yellowish in color but clear. One of the latter exhibited spontaneous coagulation, the so-called syndrome of Froin.[9]

CYTOLOGY

Of the 43 fluids, 15 showed a great increase; 24 a moderate increase and 4 no increase in cell content. Of the latter, one was from a paralytic case, fifteenth day of disease, with a 4 + albumin and a 3 + globulin reaction; another from a paralytic case, sixth day of disease, with no increase in albumin or globulin; one from an encephalitic or meningitic case, third day of disease, with a 1 + albumin and globulin reaction.

The small mononuclear cell or lymphocyte predominate in all but five fluids, viz., 88 per cent., in proportions varying from 60 to 100 per cent. These five show 95 per cent., 85 per cent., 75 per cent., 70 per cent. and 60 per cent. polynuclears, respectively. Of these, three were withdrawn on the third, fourth and fifth day of the disease. Of the two remaining, the date of withdrawal is unknown. Eight other

9. Froin and Foy: Gaz. d. höp., November, 1908.

fluids in which the small mononuclear predominates show a polynuclear content of from 15 to 40 per cent.

A cell that has been increasingly attracting our attention is the large mononuclear or perhaps endothelial cell. Many of them contain larger and smaller deep staining granules in their rather generous proportion of cytoplasm. This type is a rather rare find in fluids of tuberculous meningitis, in which fluids the cells are practically all of the very small mononuclear variety, with a hardly discernible rim of cytoplasm around the nucleus. We have also seen cells with polyform nuclei, described by Flexner and Lewis[10] as being present in a fluid of experimental poliomyelitis in the incubation and prodromal periods. When we find the large mononuclears in appreciable numbers in a smear from a clear fluid, we think of poliomyelitis. While we do not consider this type of cell pathognomonic of poliomyelitis, yet their presence warrants a strong suspicion of poliomyelitis.

As 65 per cent. of our fluids are from patients in the first week of the disease, we were unable to trace any relationship between cell content and stage of disease. There was no increase in cells in 3 fluids of the first week and in one of the second week; a moderate increase in 14 of the first week; 3 of the second week; in 1 of the third week. There was a great increase in 7 of first week; in 3 of second week; 2 of third week and in 1 of fourth week.

BACTERIOLOGY AND ANIMAL INOCULATION

Examination of smear for organisms, particularly the tubercle bacillus, has been uniformly negative. Cultures have been sterile except for an occasional evident contamination. Animals inoculated with 5 to 10 c.c. of the fluid have, after 4 weeks, borne the injection of 1 c.c. of concentrated crude tuberculin without lethal effect.

CHEMISTRY

All but three fluids showed increase in the albumin and globulin content. These three were from cases in the first week of the disease.

Our findings, on the whole, show a higher albumin and globulin content in the encephalitic cases than in those of the myelitic type. This is true particularly of the nonparalytic encephalitic variety, in which the meninges are no doubt more actively involved in the inflammatory process. Of the 17 fluids in this nonparalytic encephalitic group, four show 4 + albumin and globulin; one 3 +, seven 2 +, four 1 + and one negative albumin and globulin. Of the 4 paralytic encephalitic fluids three showed 1+ albumin and globulin and one 3 + albumin and globulin. Of 16 myelitic fluids only one exhibited a 4 +

10. Flexner and Lewis: Jour. Am. Med. Assn., 1910, liv, 1140.

albumin and globulin. This was a heavy yellow fluid that coagulated spontaneously. Of the remaining 15, two had 2+ albumin-globulin; twelve 1 + and one negative albumin-globulin. The six fluids from abortive myelitic cases all showed a 1 + albumin-globulin content. The findings of increased albumin and globulin content in the encephalitic type of fluid approach those encountered in tuberculous fluids, though 4 + albumin and globulin are comparatively fewer in the latter type of fluid. This tends to increase the difficulty of differential diagnosis.

TABLE 1.—ALBUMIN-GLOBULIN CONTENT OF CEREBROSPINAL FLUID IN DIFFERENT TYPES OF POLIOMYELITIS

Type	Albumin-Globulin					Total
	—	+	++	+++	++++	
Nonparalytic encephalitic..	1	4	7	1	4	17
Paralytic encephalitic..	0	3	0	1	0	4
Myelitic	1	12	2	0	1	16
Abortive.....	0	6	0	0	0	6

TABLE 2.—RELATION OF ALBUMIN-GLOBULIN TO DURATION OF DISEASE

Duration Disease	Relation of Albumin-Globulin to Duration of Disease					Total
	—	+	++	+++	++++	
First week....	2	18	7	1	2	30
Second week..	1	3	2	1	1	8
Third week...	0	2	2	1	0	5
Fourth week..	0	1	0	0	1	2

We could find no definite relationship between the albumin-globulin content and duration of the disease. However, our findings do show that of 21 fluids that gave a 1 + albumin-globulin, 80 per cent. were from cases under 8 days' duration, whereas of 18 fluids that gave 2 + or better, only 40 per cent. were from cases under 8 days' duration; while 3 fluids that had no increase in these contents were respectively of 3, 6 and 9 days' duration. From these figures one might infer, not too definitely to be sure, that albumin and globulin are on the increase in the later stages of the acute disease. This is in harmony with the findings of the Rockefeller Institute workers. They also find that there is a gradual diminution in the globulin content in the more chronic stage of the disease.

RELATION OF CELL CONTENT TO ALBUMIN-GLOBULIN CONTENT

Of the four fluids showing no increase in cells, one, a yellow fluid, shows a 4 +, one a 1 + and 2 no albumin-globulin. Of 22 fluids showing a moderate increase in cells, one shows a 4 +, one a 3 +, five 2 + and fifteen 1 + albumin-globulin. Of seventeen with a great increase in cells three show 4 +, three 3 +, three 2 + and eight 1 + albumin-globulin. From these findings one could infer that the cell content parallels that of albumin and globulin. These figures agree with those of Forbes but differ from those of the Rockefeller Institute workers, who found two types of fluid, the one with high cell and low globulin in the early part of the acute stage, and the other a low cell and a high globulin in the later part of the acute stage. Our report deals largely with fluids from encephalitic or meningitic cases, which may account for the discrepancy.

Interesting to note is the fact that all three of our yellow fluids gave a 4 + albumin-globulin test, and that two of them that were tested with reduction of Fehling's solution gave only a very slight reduction.

TABLE 3.—RELATION OF CELL CONTENT TO ALBUMIN-GLOBULIN

Cell Increase	Relation of Cell Content to Albumin-Globulin					Total
	—	+	++	+++	++++	
None	2	1	0	0	1	4
Moderate	0	15	5	1	1	22
Great	0	8	3	3	3	17

REDUCTION OF FEHLING'S SOLUTION

Only fifteen of our fluids were subjected to the test of reducing Fehling's solution. All of them reduced, but not in equal degree. Twelve gave a 3 + or maximum reduction and three a 1 + or minimum reduction. The relationship existing between the reduction of Fehling's and the albumin-globulin content is quite definite. The three fluids which show a 1 + Fehling's, show a 4 + albumin globulin, whereas of the 12 that show a 3 + Fehling's, none exceed 2 + and most of them show a 1 + albumin-globulin test. This relationship, in our experience, is common to all pathologic fluids. The presence of the reducing substance in varying degree, or its total absence, is the most important of chemical reactions of spinal fluids from the view point of prognosis. Thus we are able to say of a case of meningococcic meningitis before the fluid is free of organisms, that the inflammatory process is receding, by noting the return of the reducing substance.

Vice versa, we regard unfavorably a purulent fluid that clears up without the return of the reducing substance. In tuberculous fluids, its presence or absence indicates the extent and severity of the inflammatory process. A fluid that fails to reduce indicates an extensive and severe pathologic change.

DIFFERENTIATION OF CLEAR FLUIDS

The clear fluids besides those of poliomyelitis that we meet with in our work are obtained from cases of meningism accompanying pneumonia, the acute infectious diseases, and some cases of gastro-enteritis; from cases of tuberculous meningitis and from an occasional case of epidemic meningitis in which the patient is recovering. We have met with one opalescent fluid from an atypical case of rabies that strongly resembled polioencephalitis. This fluid presented a high polynuclear count and no organisms in smear and culture, comparatively low albumin-globulin and good reduction of Fehling's solution. We called it polioencephalitis until animal inoculation of the brain material proved it to be rabies.

We experience no difficulty in determining a fluid from a case of meningism, as it uniformly, in our experience, shows no increase in cells, no albumin-globulin, and a prompt and heavy reduction of Fehling's solution. Lucas[11] includes this type of fluid as presenting a cell picture similar to that found in encephalitis, poliomyelitis and tuberculous meningitis. With this we do not agree, as in none of our meningism fluids have we found an increase in cells.

The spinal fluids of patients recovering from epidemic meningitis present considerable difficulty in differentiation. They are, however, distinctly more turbid than the poliomyelitis fluids; there is a persistence of a high polynuclear content; high albumin-globulin test. These findings in conjunction with the clinical features of the case tend to clear the diagnosis.

The fluid that presents the greatest difficulty, and this is many times insurmountable, is that of tuberculous meningitis in which the tubercle bacillus has not been found. Of our last 43 tuberculous fluids the organism was found 23 times, or 53 per cent. All but one of these fluids were clear. All had a preponderance of the small mononuclear cell, 85 per cent. to 100 per cent. of the total count. Comparatively few presented the large mononuclear cell, and when present, only in small numbers. Five had 1 +, eighteen 2 +, sixteen 3 + and four 4 + albumin-globulin. The behavior towards Fehling's solution is quite different from that of poliomyelitis fluids. Twelve produced no reduction; 21 only a very slight reduction, 6 a 2 + and 4 a 3 + reduction.

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11. Lucas: Am. Jour. Dis. Child., 1911, i, 230.

TABLE 4.—Showing Albumin-Globulin Content and Reduction of Fehling's Solution

	Albumin-Globulin						Reduction of Fehling's Sol.				
	—	+	++	+++	++++	Total	—	+	++	+++	Total
Poliomyelitis	2	25	9	2	5	43	0	3	0	12	15
Tb. Meningitis...	0	5	18	16	4	43	12	21	6	4	43

It is to be noted also that the albumin-globulin content is higher in the great majority of tuberculous fluids. Approaching these in this respect are the fluids of the encephalitic group. Hence, a clear fluid, free from tubercle bacillus, with a high small mononuclear count, comparatively high albumin-globulin content and low in reducing substance, is more apt to be tuberculous than poliomyelitic.

A very important point in determining the diagnosis of a case with the fluid findings described as being present in either poliomyelitis or tuberculous meningitis is to be had in the history of the case. If there is an acute onset with high fever, 103 to 104, in a previously healthy person, we do not hesitate to make a tentative diagnosis of poliomyelitis. Sudden onset in tuberculous meningitis is an exceedingly rare occurrence. An excellent table of differential points in the examination of spinal fluids has been furnished by Du Bois and Neal.[12]

As to the value of lumbar puncture and examination of the spinal fluid, too much cannot be said in its favor. It can be made the means of clearing up the diagnosis in puzzling cases presenting meningeal or cerebral symptoms. Peabody, Draper and Dochez,[8] Lucas[11] and Frissel,[13] present evidence of definite aid in 18 cases of poliomyelitis in the preparalytic stage. The technic of lumbar puncture is simple and safe and the examination of the fluid is not complex.

CONCLUSIONS

1. The cerebrospinal fluids of poliomyelitis and encephalitis show abnormal changes in practically all our cases.

2. The fluids of poliomyelitis and encephalitis present no specific characteristics.

3. Fluids from cases of encephalitis generally show a higher albumin-globulin content than do the fluids of myelitis or of the abortive cases.

4. Fehling's solution is reduced by all fluids but not in equal degree.

5. Examination of the spinal fluid is the most important factor in clearing up the diagnosis in abortive and preparalytic cases.

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12. Du Bois and Neal: Summary of Four Years of Clinical and Bacteriologic Experience with Meningitis in New York City, AM. JOUR. DIS. CHILD., January, 1915, ix, 1.

13. Frissel, L. F.: Jour. Am. Med. Assn., 1911, lvi, 661.

A CLINICAL STUDY OF TWO HUNDRED AND TWENTY-EIGHT CHILDREN IN RELATION TO TUBERCULOUS EXPOSURE CONTROLLED BY VON PIRQUET REACTION *

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This paper represents a clinical study of 228 children coming under our observation during the past two years as volunteer workers in the Saturday morning children's clinic of the tuberculosis division of the Seattle Department of Health. It should be understood at the outset of this paper that these children represent a group in the community most likely to give evidence of tuberculous infection, since the large majority are children from tuberculous homes. Many other children were seen who cannot be included in this series owing to the incompleteness of their records. The reasons for this are unavoidable, since many children come to the clinic but once, and no opportunity is given either for the observation of the von Pirquet test or to confirm any conclusion reached at the time of the first visit. For purposes of convenience in the filing and handling of records in the clinic some definite classification of these cases must be made. Every one coming in contact with tuberculosis in childhood and infancy realizes the difficulty, in many instances, which is attached to making a diagnosis. Unless the classification is very general and permits of considerable elasticity, it is likely only to be a source of confusion, since the interpretation of a case often depends to a large extent on the individual inclination of the examiner. Finer degrees and shades of impaired resonance, finer degrees of prolonged expiration, finer shades of harsh breathing and of paravertebral dulness, we all realize are rather uncertain findings on which to form an exact basis of classification.

CLASSIFICATION IN USE IN THE CLINIC

We have divided our cases in the clinic into three general groups, (1) tuberculous, (2) clinically non-tuberculous, (3) non-tuberculous. The tuberculous children represent those children giving clinical evidence of tuberculosis with or without a positive von Pirquet. Clin-

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ically non-tuberculous, those children giving no clinical signs but giving a positive von Pirquet. Non-tuberculous being those children giving no clinical signs and a negative von Pirquet.

There is a large number of cases constantly carried along in the files with diagnosis deferred. These records form that group previously referred to as being unusable in this series. While the above classification is the one in use in the clinic at present, for the purpose of this paper, which is a study in relation to home exposure, these cases have been tabulated somewhat differently: 1. Children with a definite history of exposure. 2. Children with no history of known exposure.

We assume that in a large series of cases such as this, for all practical purposes the cutaneous tuberculin reaction of von Pirquet is nearly as reliable as the *stichreaction*. Veeder, in a recent study of 1,321 children in St. Louis, reached the conclusion that the intradermic tuberculin reaction gave but a slight increase in the percentage of positive cutaneous reactions. The von Pirquet test is made by the nurse, but under our supervision, with one-half strength "old tuberculin." Since these reactions have been carefully made, when they were negative in many instances they have not been repeated. It is difficult in a clinic of this sort to retest each negative reactor, no matter how desirable it might be to do so. Several negative reactions have been repeated once and in some instances twice without change. I feel sure that subsequent cutaneous tuberculin tests made within a short time on those giving a negative reaction at first examination, would have altered our series only to a limited extent. There are 166 children out of the 228 who have been or still are living in intimate contact with active adult cases. In the remaining sixty-two there is no known exposure. These adult contacts, in most instances, one or the other parent, in a few instances both parents, or older brothers or sisters, are in the stage of lung invasion in varying degrees of activity. As many as can be have been segregated at the new City Tuberculosis Hospital at Firland.

CHILDREN WITH A DEFINITE HISTORY OF EXPOSURE

There are eighty-four of the 166 children with a definite history of exposure who give a positive von Pirquet test, or about 50.6 per cent. Of this number, as naturally would be expected, the largest part, sixty-nine, or 82.1 per cent., shows no clinical evidence of tuberculosis. It has for some time been the teaching that tuberculosis in an infant progresses rapidly toward a fatal termination. More recently, however, Halm, Ibrahim and Eichelburg have reported cases to prove that prognosis is not absolutely bad in infants. While these children of the clinically non-tuberculous group bear their infection with the tubercle

bacilli without apparent harm, their systems probably being proof against the organism, nevertheless, we attempt a close observation of these children. Each few weeks they return. We have been unfortunate enough in a few cases to observe an inactive tuberculosis assume alarming evidences of activity, even among older children. There are a few from this group, nine in all, in whom one of us nas recorded questions of finer shades of impaired resonance or harsh breathing, where one did not at the same time seem justified in regarding such indefinite findings as constitutional signs. It would probably be better to classify these clinically non-tuberculous children as suspicious. There are fifteen children, representing 17.8 per cent. of those children exposed to tuberculosis, who give a positive reaction and clinical evidence of tuberculosis. They show varying degrees of activity and types of infection, including seven cases of bronchial gland tuberculosis, one active keratitis, two with cervical adenitis, four with distinct lung invasion, and one with tuberculous peritonitis. Since this paper was undertaken, one inactive, clinically non-tuberculous child developed an active tuberculous peritonitis right under our personal observation.

Most of those diagnosed as bronchial gland tuberculosis are children with a distinct history of not doing well, with subnormal or slightly elevated temperature, frequently complaining of pain in chest or back, poor appetite, weakness or listlessness, with dilated chest veins, but no physical evidence of tuberculosis except sometimes paravertebral dulness. Radiographs showed corresponding shadows about the right hilus. The absence of any bone cases is due to the fact that we have in Seattle a splendid orthopedic hospital, the Children's Orthopedic Hospital, and cases of that character are early recognized and sent to that institution.

There were eighty-two children with a definite history of exposure who gave a negative von Pirquet. This represents about 49.3 per cent. who give negative reactions out of the total 166 exposed to tuberculosis. One of these children gives distinct clinical evidence of tuberculosis, in which instance, as would be expected, the process has advanced to the third stage. There are eight in whom one of us recorded questions of finer shades of harsh breathing. In view of the fact that cutaneous reaction is negative in the presence of measles, it is only fair to state here that none of these children had measles at this time or within recent date.

CHILDREN WITH NO HISTORY OF EXPOSURE

The children we have just been considering were children sought out and brought to the clinic especially, by the nurses of the department, owing to their known intimate contact. These sixty-two children whom we now consider, were brought to the clinic because of

poor nutrition, or by fear that something of the nature of tuberculosis might be present, rather than because of any known exposure. Fourteen of these sixty-two children, or about 22.5 per cent., give a positive von Pirquet, the remaining forty-eight, or 77.4 per cent., give a negative test.

TABLE 1.—REACTIONS OF EXPOSED AND NON-EXPOSED CHILDREN

	Positive von Pirquet		Negative von Pirquet	
	No.	Per Cent.	No.	Per Cent.
166 children exposed	84	50.6	82	49.3
62 children with no known exposure	14	22.8	48	77.4
228 children	98	42.9	130	57.1

It is interesting to note in Table 1 that in the entire series of 228 children, with so large a number having known exposure, the percentage of positive reactions was only 42.9 per cent.

The assertion made by Fishberg[1] that the difference between those who lived in a tuberculous *milieu* and those who had no contact with consumptives in their homes, is apparently insignificant, cannot be borne out by this series. In fact, decidedly the contrary is the case. One encounters many interesting problems in such a series as this, where children exposed to a tuberculous mother and father who are in active stages of lung invasion, should react negatively with every opportunity of infection. Again, one child with equal exposure yields a negative reaction, while all the other children in the family react positively.

In considering the entire series by ages, as a majority of similar investigators have done, we have the results shown in Table 2.

TABLE 2.—RESULTS IN THE SERIES BY AGES

Age	Number Tested	Per Cent. of Positive Reactors	
Under 1 year	7	2	28.5
Under 2 years	10	7	70.0
Under 3 years	12	4	33.3
Under 4 years	33	15	45.4
5 to 7 years	37	13	35.1
7 to 10 years	58	17	29.3
10 to 15 years	70	40	58.1

The high percentage of positive reactions under two years is due to the fact that the whole number (10) is not large and nearly all of these were brought in because of a death recently of one or the other parent. Otherwise, the series corresponds in general with similar studies illustrating the fact that the reaction gradually becomes more frequently positive until 10 to 15 years of age, where the maximum is reached.

1. Fishberg: On the Cutaneous Tuberculin Test in Children of Non-Tuberculous Parentage, Arch. Pediat., 1915, xxxii, 20.

REVIEW OF SIMILAR STUDIES

For purposes of convenience in contrasting these similar studies we have followed the grouping of our cases in a general way with von Pirquet's proposal for an international statistical study of the frequency of tuberculous infection in children. There are many extensive articles on different phases of the cutaneous tuberculin reaction in children, in which this aspect has been neglected or only slightly touched on, which are not usable.

Tabulating for purpose of convenience these similar studies, we have the results shown in Table 3.

TABLE 3.—STUDIES OF TUBERCULOUS REACTION IN CHILDREN

Name	No. of Children Tested	Age at which Largest Percentage of Positive Reactions Are Obtained, Years	Percentage of Reactions
Von Pirquet[2]	1,407	13-14	93.0
Hamburger[3]	532	13-15	95.0
Hellesen[4]	480	10-14	46.0
Shaw and Laird[5]	330	over 6	45.0
Meroz and Khalatoff[6]	337	10-15	78.6
McNeil[7]	541	4- 5	45.0
Sachs[8]	217	10-15	60.0
Berberich[9]	800	10-15	58.8
Lapage[10]	1,000	5-10	60.8
Arieti[11]	38	7-11	59.0
Fishberg[12]	692	14	83.79
Fishberg[1]	588	14	75.0
Veeder and Johnson[13]	1,321	10-14	44.0
Manning and Knott	228	10-15	58.1

Fishberg's two series and our own were studied particularly in relation to tuberculous exposure.

COMMENTS ON INFLUENCE OF COMMUNITY CHARACTERISTICS OF CLIMATE, HOUSING, SANITATION, ETC.

The disparity of results obtained by various observers cannot be easily explained. T. Frazer[14] is of the opinion that discrepancies must be attributed to differences of technic and to an agreement as to

2. Von Pirquet: Jour. Am. Med. Assn., 1909, lii, 675.
3. Hamburger: Med. Klin., March 30, 1913.
4. Hellesen: Jahrb. f. Kinderh., June 12, 1909.
5. Shaw and Laird: Arch. Pediat., 1909, xxvi, 488.
6. Meroz and Khalatoff: Rev. méd. de la Suisse romande, 1914, xx; abstr. Arch. de méd. des enf., 1913, xvi, 307.
7. McNeil: Edinburgh Med. Jour., 1912, viii, iv, 324.
8. Sachs: Trans. Internat. Cong. Tuberc., 1908, ii, 484.
9. Berberich: Abstr. Arch. de méd. des enfs., 1913, xvi, 307.
10. Lapage: Brit. Jour. Child. Dis., 1912, ix, 497.
11. Arieti: La Pediatria, 1913, iii.
12. Fishberg: Arch. Pediat., 1914, xxxi, 96.
13. Veeder and Johnson: AM JOUR. DIS. CHILD., 1915, ix, 478.
14. Frazer, T.: Med. Rec., New York, 1915, lxxxvii, 2, 57.

what constitutes a reaction; as different methods of scarifying, the depth of abrasion, the concentration of tuberculin. The technic is so simple that this factor, we believe, differs very slightly in any carefully observed series. The assertion has frequently been made that nearly all children at 15 years of age are tuberculous. In support of such an assertion the figures already incorporated into this paper, of Hamburger and von Pirquet especially, are quoted. What right have we, however, to assert that what is true of Vienna is true of our own community? One of us (M.) has seen both of these clinics and spent a month in Hamburger's, and has never seen in any clinic so many children with third stage tuberculosis as in Hamburger's clinic. Rather than differences in technic must we believe of far more importance in explaining difference of frequency of tuberculosis in children in different communities, are peculiarities of climate, sanitation and housing of these different communities. Children frequenting the Poliklinik and the Kinderklinik in Vienna come from poorly heated, poorly ventilated, stone houses standing side by side, row after row of five story buildings. Many of these buildings and rooms standing years, probably have been inhabited by more than one generation of consumptives. This situation contrasted with the community characteristics of a new community like our city, must explain these discrepancies. In a climate favorable to open air living, with a community made up of separate houses, and furthermore, with each home a comparatively new, modern house, and probably few, if any, over twenty-five years of age, the number of community foci of tuberculous infection must be far less in Seattle than in Vienna.

CONCLUSION

In a clinical study of 228 children in relation to tuberculous exposure controlled by the cutaneous von Pirquet test, we find that, contrary to the findings of Fishberg, children living in tuberculous *milieu* and those with no known contact with consumptives show marked differences; those living in tuberculous surroundings reacting in ratio of about 2 to 1 of those living in an environment not known to be tuberculous. Further, we find the number of positive reactors in the entire series is only 42.9 per cent. We also find that the number of children between 10 and 15 years reacting positively to the cutaneous tuberculin reaction, in a series in which the majority of the children are from tuberculous homes, is 58.1 per cent., far below the figures of Hamburger, 95 per cent., and von Pirquet, 93 per cent.

These discrepancies are due, in our opinion, to community characteristics of climate, housing and sanitation.

A CONGENITAL MALFORMATION OF THE INTESTINE

MULTIPLE POINTS OF COMPLETE OBSTRUCTION

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According to various authors, congenital malformation of the intestine is not very frequent, aside from imperforate anus. When the rectal malformations are left out of consideration it is stated that the large bowel is much less commonly the site of congenital variations than the small bowel.

Leichtenstern[1] found the proportion of cases in the different situations as follows: 375 at the anorectal junction, 75 in the small intestine, and 10 in the colon.

Holt[2] says that stenosis or atresia may occur at one or more points in the small bowel, but that obstruction is much more frequent in the upper portion, the common seat being the duodenum. Atresia is more often seen than stenosis, the causes suggested for their formation being fetal peritonitis and volvulus.

A review of the literature indicates that but one point of actual obstruction is usually found, while beyond this are sometimes found one or more points of stenosis. The clinical picture produced by such a malformation is that of intestinal obstruction and, as a rule, even surgical intervention can offer little hope of a cure. The duration of life depends on the location of the obstruction. The nearer the stomach the lesion is, the shorter the duration of life.

In view of the infrequency of this condition, and because of the very limited number of cases, if any, of complete multiple congenital obstructions of the jejunal type, we offer this brief case report taken from the surgical service of Dr. A. B. Herrick.

CASE REPORT

Hospital No. 169112, Baby S., white, male, aged 4 days, local residence, Paraiso, Canal Zone.

Family History.—Mother and father in good health; no accident to mother during gestation, so far as could be determined. First childbirth normal and the child continues in good health up to the present. No family history of such an accident in either the maternal or paternal records.

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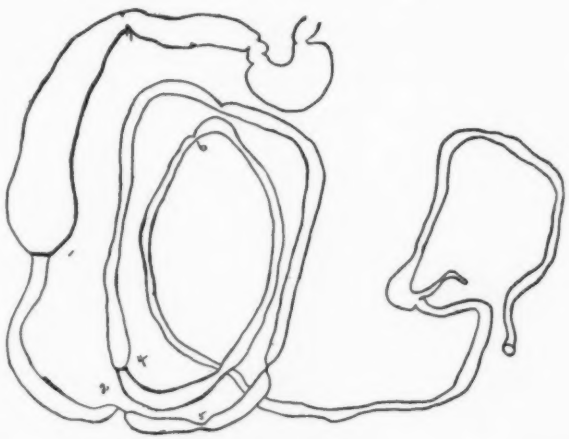
1. Leichtenstern: Osler's Modern Medicine, Lea & Febiger, Philadelphia and New York, 1908, v, 458.
2. Holt, L. E.: The Diseases of Infancy and Childhood, D. Appleton & Company, New York and London, 1909, p. 353.

Previous History.—The child was born on November 15 at 3 p. m., after a normal, easy delivery. Vomiting began as soon as the child was put to the breast and was repeated after every feeding. The vomited matters were bile-stained mucus and milk. On account of the fact that the bowels did not move, on the following day calomel was given without result, and after an enema a small amount of inspissated meconium was passed. The vomiting continued until the child was brought to the hospital. Repeated enemas were given without result. The urine was normal.

The infant was put to the breast regularly and given about a dram of warm water after each feeding. All feedings were retained about four hours and then a small amount of milk was regurgitated. Three hours later it had another attack when about four ounces were vomited in somewhat of a projectile manner. Little vomiting attacks then continued at intervals and the child became fretful. The day following its birth the infant appeared dull, listless and was somewhat jaundiced. A loss of four ounces in weight was noted. There was



The bowel was fixed in a formaldehyd solution and then arranged so that an exact tracing could be made of its shape and length. This tracing was then photographed and the figure presents, on a smaller scale, the true relations of the stenosed and obstructed points. There were three compartments in the small bowel that were entirely closed at either end. Other points of stenosis were apparent at 5, 6, 7, etc., as indicated in the figure. The entire length of the small bowel was 175 cm., that of the large bowel 30 cm.

no bowel movement. Congenital obstruction was suspected and Dr. Herrick advised and performed a laparotomy. Exploration revealed a high congenital malformation causing complete obstruction of the small bowel, and other points indicating stenosis of the small intestine. Surgical interference appeared hopeless and further operative efforts were abandoned. The abdomen was closed and the child removed to the ward. Death occurred a few hours later.

Necropsy.—A small, male, white child; skin and conjunctiva jaundiced; head not examined. Nothing abnormal was found in the thoracic or any of the abdominal organs excepting the gastro-intestinal tract.

The stomach appeared normal but the peculiar formation and arrangement of the large and small bowel necessitated a careful removal and rearrangement before all segments could be recognized.

Four complete congenital occlusions of the small bowel were found. The first one was 28 cm. from the pyloric ring and the form of occlusion was that

of a thin tissue diaphragm lined on its upper surface by the usual type of mucous membrane, while below, it had a smooth parchment-like surface. The duodenum and the portion of the jejunum above this partition had been a large food reservoir for all the food taken, and therefore was tremendously dilated and the wall thickened. This portion of the bowel and that which immediately followed it were so modified in appearance that the first impression on opening the abdomen was that some peculiar transposition of the viscera had taken place, because it resembled a large cecum and appendix. This enlarged portion had gravitated to the right iliac fossa. Only a complete dissection of the esophagus, stomach and bowel allowed a proper orientation.

The second obstruction was found 15 cm. below the first one mentioned, but instead of a membranous partition the bowel simply tapered off to a fine solid cord of tissue measuring 3 or 4 mm. in length and about 1 mm. in diameter. No food had ever had access to this portion of the bowel. The content was a clear, mucous fluid.

The third obstruction was 10 cm. below the second one just described and was similar in nature.

The fourth obstruction was 42 cm. below the third and was a membranous partition like the first one described except that the segment of the bowel and the partition were of course small. On the peritoneal coat there was no evidence of this occlusion and even though the surgical intervention had removed the first, second and third obstructions, this one would have defeated their efforts. This point was found only by injecting water through a syringe into all portions of the bowel to see how many compartments really existed.

When water was injected above the first obstruction it eventually escaped through the stomach and esophagus and when injected below the fourth obstruction it escaped through the large bowel by way of a catheter in the rectum. No imperforate state of the ano-rectal region existed.

No evidence of a congenital malformation was found in the body other than a small, persistent foramen ovale.

The case not only presents an unusual number of congenital malformations in the jejunum but shows how difficult and hopeless surgical treatment may be under such conditions.

INTESTINAL PARASITES IN CHILDREN*

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The subject of intestinal parasites in children is one that I believe has not been given the care and attention that it rightly deserves. Generally speaking, only those patients are examined for parasites who come with a definite history referable to the parasites, such as the finding of a segment of tenia in the stools, or when the mother of the patient makes the statement that she believes that her child has worms, do we ask for a specimen and examine or have the stools examined.

That this was true was forcibly brought to my attention by the number of cases that came to me, both in my private practice and in the West End Dispensary, either with the statement by the mother that the child had worms, or with the child complaining of other symptoms not referable to a parasitic disease; yet on routine examination these cases were found to harbor one or more of the different parasites to be mentioned later.

Although the Rockefeller Hookworm Commission had as thoroughly and systematically worked the state by counties as was possible with funds and time available, I determined to study the subject through the children that came under my observation in my clinic, at the Masonic Home, and also through the courtesy of Dr. P. B. Moss, State Pathologist and Bacteriologist, the children under the age of 12 years who came to the State Pasteur Institute to be treated for dog bites.

My observations include all those children who were at the Masonic Home or who came to the clinic or Pasteur Institute, regardless of the nature of their complaints. Some of them, especially the cases from the Home and Pasteur Institute, did not complain of any untoward symptoms whatsoever. In fact, they were perfectly healthy specimens whose parents would never have thought to consult a physician had it not been for the accidental bite of a supposedly rabid dog and their fear of hydrophobia. These observations cover a period from Septem-

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ber, 1910, to March, 1915, in the Pasteur Institute, and from May, 1914, to April, 1915, in my own dispensary and Masonic Home. (The examinations were made in the State Laboratory by Dr. P. B. Moss or one of his assistants). The total number of children examined being 665, 80 of whom were negroes, and all under 12 years of age. Of this number 240 were found to be infected; 425 negative, or 36.1 per cent., of the children were found to harbor one or more of the varieties of parasites as follows:

Hookworms	177	(62 F. 115 M.)	26.75%
Hymenolepis nana	38	(20 F. 18 M.)	5.75%
Ascaris lumbricoides	27	(12 F. 14 M.)	4.06%
Oxyuris vermicularis	5	(3 F. 2 M.)	.75%
Trichocephalus dispar	5	(2 F. 3 M.)	.75%
Mixed infections 2 or more parasites	12	(6 F. 6 M.)	1.8 %

Amoeba coli and *Amoeba histolytica* will not be considered here.

Of these infections it will be noted that three children of one family had a double infection of *Ascaris lumbricoides* and *Trichocephalus dispar*. In one family one child was infected with hookworm and *Hymenolepis nana* while the second had hookworm only. In the third family one child was infected with *Hymenolepis nana* and *Trichocephalus*. In still another, one child was infected with *Hymenolepis nana*, with both hookworm and *Hymenolepis nana* in the second.

It is a common occurrence to find whole families infected with hookworm, while in five families *Hymenolepis nana* was found in two or more members. In many cases it was only possible to examine one child of a family or I believe this number would be largely increased.

It is to be remembered that very few of these patients complained of any untoward symptoms due to the parasites, but as before stated, came to the Pasteur Institute to be treated for dog bites, or to the dispensary for any of the ordinary diseases that usually come to a dispensary or free clinic.

It might be well to mention here that of the patients presenting themselves to the Pasteur Institute 34.5 per cent. were infected. Many of them came from Birmingham, Mobile, Montgomery, Selma and the larger centers of population of the state where hookworm infection is not so common as in the rural districts and medical attention is much easier to obtain, and where had they complained of any symptoms referable to the parasites, they would more than likely have been discovered and treated.

Therefore, the percentage of intestinal parasites in children of the state as a whole may be considered even larger than have been found here.

The large percentage of parasites which apparently give no untoward symptoms might easily lead one to believe that they are of

little relative importance to the health of the child. That such is not the case I have proved to my own satisfaction by treating several children complaining of abdominal pains, loss of appetite, tired, listless feeling, etc., and giving them a thorough treatment, watching the marked improvement in the general condition and the disappearance of symptoms complained of. Especially was this so in some of the children of the Home. Several of these when admitted were pale, sallow, undeveloped, listless children with no appetite, and yet did not complain of any specific illness. Examinations of feces showed severe, neglected infection in some cases of more than one variety of parasite. They were first given a course of treatment for hookworm and allowed to rest from one to two weeks, when the feces were again examined; if they showed any infection they were given a second treatment. All that had showed signs of infection were re-examined in four weeks, and if necessary, treated again. It is my intention to have these children given a routine examination in six months and to repeat the treatment wherever necessary.

Although I have had these children in charge for over one year, since the eradication of the parasitic infection there has been very little illness at the home. Those who were infected, after treatment took on a different aspect. They lost their sallow complexion, regained appetite and became as other children.

I have made no effort to go into the etiology, symptomatology or treatment for these parasites, but to find out the percentage of children infected and the relative proportion of the different parasites found on routine examination.

It was not surprising to find hookworm to be by far the commonest of the infections, especially in this section, but the large percentage of *Hymenolepis nana* and *Ascaris lumbricoides* and the small number of *Oxyuris vermicularis* was somewhat of a surprise,[1] as the *Oxyuris* has been considered quite common, especially by the parents of the patients, while the *Hymenolepis nana* was considered comparatively rare.

There can be no doubt of the importance of ridding the children of these parasites, as they are undoubtedly a factor in the malnutrition and poor development of many, and may be a predisposing cause of pellagra, tuberculosis, dysentery, subacute and chronic appendicitis and other diseases. In thirty-five cases of pellagra under my care, thirty-one were infected with either hookworm, *Hymenolepis,* or both.

1. This bears out Schloss in his article in Archives of Pediatrics, February, 1910.

The frequency of intestinal parasites when looked for, has been shown by other investigators. Still[2] found 32 parasitic infections in 100 consecutive autopsies. Schloss[3] found 11 per cent. of the children who came to his dispensary, infected with some variety of parasite. Wilson[4] reports twenty pinworm infections in 100 consecutive necropsies in children, and other reports bear this out. Although these investigations do not show such to be the case, McNeil[5] states that pinworm is comparatively common; that contrary to the general impression, they are usually found in the small intestine, cecum, and appendix, rather than in the lower intestine. In severe infections they may travel down to the anus and be detected there if searched for, but usually they are not found in the stools unless drawn down by an active purge, and even then an active search is necessary. McNeil[5] also states that it is pretty thoroughly demonstrated that both the pinworm and the whipworm are etiologic factors in attacks of acute and subacute appendicitis, and that they probably lay the foundation for some attacks of suppurative appendicitis.

The reduction of death rate in Bilibid prison from 75 per 1,000 to 9 per 1,000 after quarantining the persons harboring intestinal parasites, seems to indicate that there is some importance to be attached to their presence.

CONCLUSIONS

1. That parasitic infections in children are far more common than has heretofore been thought.

2. That while hookworm infection is the most often found, *Hymenolepis nana* and *Trichocephalus dispar* are by no means rare.

3. That less than 10 per cent. of the cases infected complain of symptoms referable to the infection.

4. That by routine examinations, many cases will be found otherwise unsuspected and by thorough treatment their general condition will be greatly improved.

5. Every county and municipality should appoint a physician for special work along this line, to follow the work done by the Rockefeller Hookworm Commission and under the direction of the state health officer, who should at frequent intervals examine the feces of every child in his district. No child should be permitted to attend a public or private school until after such an examination and the results prove to be negative.

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2. Still: Common Diseases and Disorders of Childhood.
3. Schloss: Am. Jour. Med. Sc., 1910, cxxxix, 458.
4. Wilson: Brit Med. Jour., 1913, p. 2676.
5. McNeil: Southern Med. Jour., June, 1915, p. 487.

POLYCYSTIC DISEASE OF THE KIDNEY IN AN INFANT THREE MONTHS OLD*

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According to Kelly, polycystic disease of the kidney occurs principally at two periods of life—before or immediately after birth, or after 40 years of age. Although many cases in adults have been reported in the literature, the disease is uncommon enough in infants to warrant the publication of the following instance as well as a brief discussion of the condition.

CASE REPORT

History.—H. D., female, 3 months old, was admitted to the A. Jacobi Division for Children of the German Hospital, May 13, 1915. Forceps delivery. Weight at birth not known. Breast feedings were given every two hours. The mother has had no miscarriages. There is no family history of lues or tuberculosis. Both parents and one brother of the patient are alive and well.

Present Illness.—About two weeks after birth the mother noticed that the infant's abdomen began increasing in size. Shortly afterwards the physician who was called stated that the child had an enlarged liver. In the past two months the increase in the size of the abdomen has been progressive. There have been occasional attacks of abdominal pain, apparently most severe with the child on its back. Stools were three to four daily, and always contained mucus; blood was noticed on one occasion. Appetite has always been good. There has been no vomiting. At no time were there urinary symptoms. The urine has been dark colored at times, but the diapers were never stained. The general condition of the infant has been poor since the first month of life.

Examination.—On admission to the hospital examination showed a badly developed infant in a profoundly prostrated condition. Weight 10 pounds. Length 22½ inches (57 cm.); circumference of head 14½ inches (37 cm.); circumference of chest 14⅜ inches (36.5 cm.). The examination of the skin, eyes, ears, nose, mouth, throat, lungs and heart was negative. Very slight generalized enlargement of the lymph-nodes.

Abdomen: Markedly enlarged and distended. Circumference of abdomen at umbilicus 16 inches (40.5 cm.). A small umbilical hernia is present. In each flank a large, hard, somewhat irregular mass is palpable; the tumors extend from the costal arches into the pelvis. The inner margin of the mass on the right side feels lobulated, and appears to be continuous above with a mass extending transversely to the left and posteriorly below the costal margin.

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* From the A. Jacobi Division for Children of the German Hospital, New York.

Both masses are ballottable from the flank. Dulness is present over each. The percussion note is tympanitic towards and in the median abdominal zone. There is no moveable dulness present, and a fluid wave could not be elicited.

Liver: The edge is palpable 3 inches below costal margin; its surface feels smooth and is not tender.

Spleen: Not felt.

Rectal Examination: Negative.

The von Pirquet reaction was negative. Roentgen-ray examination (Dr. W. H. Stewart) showed an enlarged abdomen and an hypertrophied heart (Fig. 1).

Fig. 1.—Polycystic disease of the kidney, showing hypertrophied heart.

The urine contained a very slight trace of albumin and a few granular casts. No red blood cells were present. The temperature, respiration and pulse rate were normal. The blood examination showed on admission: hemoglobin, 70 per cent.; white cell count, 13,200; polynuclears, 50 per cent.; lymphocytes, 46 per cent.; eosinophils, 4 per cent.

In the absence of a luetic history, and especially because the general condition of the patient was so poor, a Wassermann test was omitted.

The chief point of interest in this case was the presence of the bilateral tumor masses in the abdomen, with the history of the evolution shortly after birth. In an effort to arrive at the diagnosis the following possibilities were considered:

1. Tuberculous peritonitis.
2. Syphilis.
3. Sarcoma of omentum.
4. Sarcoma of kidney.
5. Polycystic disease of the kidney.

Tuberculosis and syphilis were ruled out because there was no specific history, and because the symmetrical arrangement of the tumors and their presence dating from birth, spoke against these conditions. A differential diagnosis between sarcoma of the omentum and kidney tumor (malignant or cystic) could not be definitely made. As will be indicated below, bilateral abdominal tumors in an infant dating from birth, with signs of chronic kidney inflammation and an hypertrophied heart, speak very strongly for polycystic disease of the kidney. Nevertheless a positive diagnosis could not be made.

In view of the fact that the tumors were gradually progressing in size, and that the infant's condition was gradually getting worse, an exploratory operation seemed advisable. At the laparotomy, performed by Dr. F. Kammerer four days after the patient had been admitted to the hospital, the tumor masses were found to be retroperitoneal, and in the position of the kidneys. The patient died the day after the operation.

We are indebted to Dr. F. B. Humphreys, pathologist to the German Hospital, for a detailed report of the necropsy findings. The following is an abstract from his records:

Pathologist's Report.—Heart: Weight 62 gm.; hypertrophied, but otherwise normal.

Lungs: Slight congestion; no enlargement of bronchial lymph nodes.

Thymus: Weight 7 gm.

Intestines: Slight congestion. The small intestine was distended, due to partial obstruction by the tumor masses.

Kidneys: (Figs. 2 and 3.) Enormously enlarged. The right kidney weighed 240 gm., and the left kidney 230 gm. Each kidney measured 12 by 6 by 5 cm. The organs were irregularly lobulated. The capsule was firmly adherent. The section was of a light yellow color streaked with coarse vertical white striae. There was scarcely any differentiation between cortex and medulla. The kidneys were of a spongy or boggy consistency, the meshes of the sponge being filled with a clear, light-yellow fluid which could easily be expressed. There were a few good-sized cysts (3 to 4 cm. in diameter) and innumerable smaller ones (pin point in size) scattered throughout the kidneys. The mucous membranes of the calices and pelves appeared normal.

Liver: Weight 235 gm. Normal in appearance, but of unusually firm consistency. On section the connective stroma was increased, the normal liver tissue being replaced by a firm white network resembling connective tissue. Small brown islands were enclosed in the latter.

Microscopic Examination.—Kidneys: Almost the entire parenchyma was made up of exceedingly irregular epithelium-lined spaces of varying sizes. No resemblance to the normal renal tubules was discoverable. The normal histologic landmarks were almost completely obliterated; glomeruli and nondilated tubules were found in isolated groups irregularly scattered in the connective tissue between the spaces. For the most part, however, the spaces were bare. The epithelial cells referred to were of the flattened cuboidal type, and were detached from the underlying basement membrane in many places. The connective tissue varied greatly in amount in different specimens. In most places

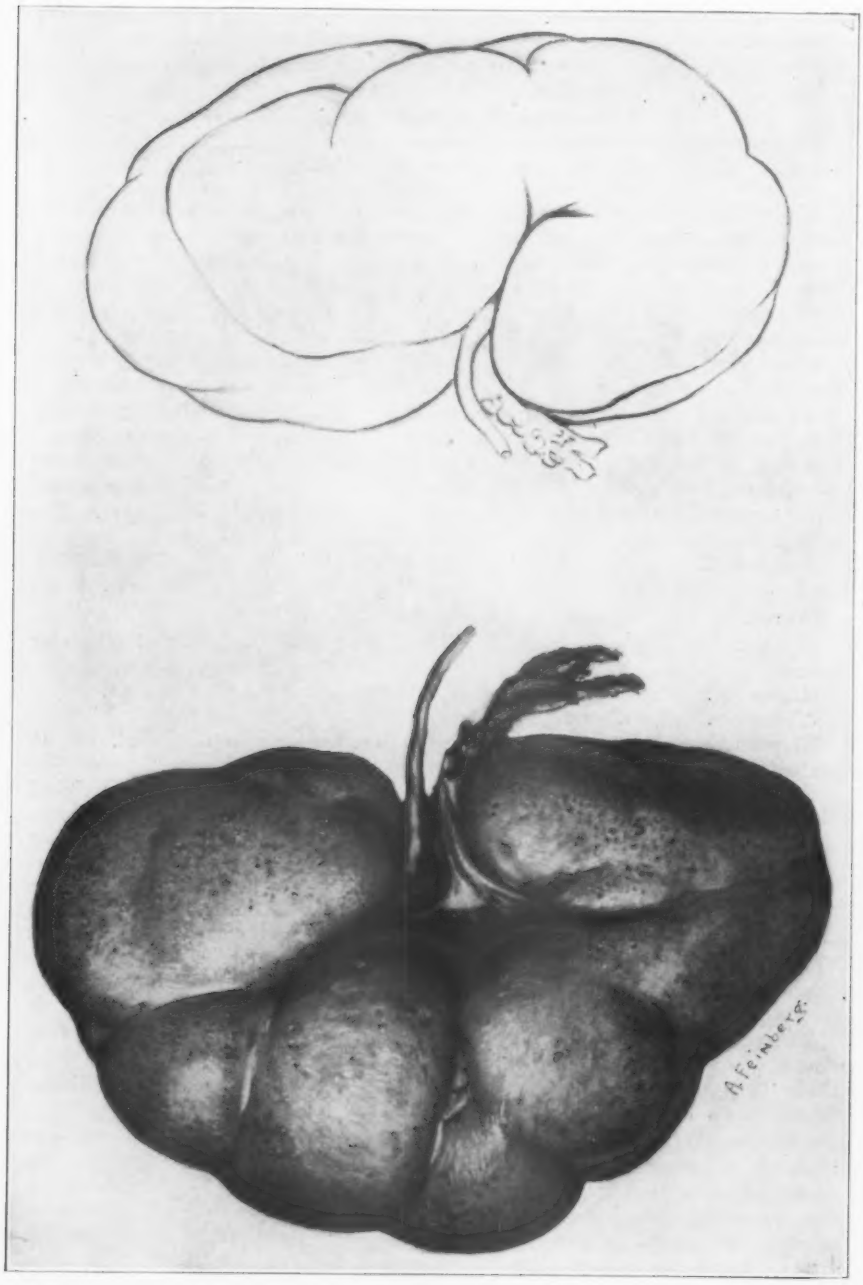

Fig. 2.—Polycystic disease of the kidney.

it was very scanty, serving only as a thin sheath for the capillaries between the dilated tubules. Imbedded in it were the approximately normal glomeruli and tubules. These areas were more numerous near the surface, where the stroma becomes continuous with the external capsule. There was no marked inflammatory reaction. Spirochetes were not found in section prepared by Levaditi's method.

Liver: The interlobular connective tissue was enormously increased in amount, its bulk approximately equaling that of the epithelial lobules. The latter were much reduced in size and formed irregular islands of varying sizes, separated by broad bands of connective tissue. There was no marked intralobular fibrosis, although there was pronounced congestion. The most remarkable feature was the hyperplasia, hypertrophy and dilatation of the bile ducts.

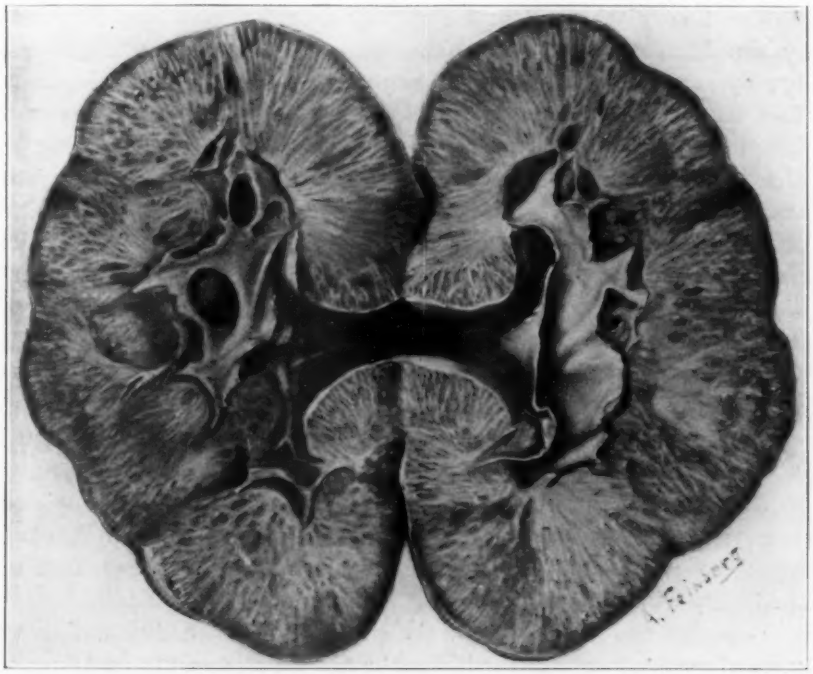

Fig. 3.—Polycystic disease of the kidney.

The interlobular connective tissue was everywhere honeycombed by large irregular intercommunicating spaces of varying sizes, lined by single rows of columnar epithelium resembling that of the normal bile passages. Some were empty; others, especially the larger ones, were filled with cellular detritus, pigment, etc. The surrounding connective tissue contained scattered areas of round cell infiltration, but showed no recent inflammatory changes. Silver nitrate impregnation after the method of Levaditi showed no spirochetes.

DISCUSSION

Etiology.—There are numerous theories concerning the etiology of cystic disease of the kidney. According to Moschcowitz the theory expounded by Virchow is the oldest one. Virchow maintained that

the cysts arose from an intra-uterine papillitis caused by irritation of uric acid and lime salts, resulting in atresia and obliteration of the collecting tubules. This is the so-called inflammatory or retention cyst theory, which has very few adherents at the present time.

Some years later, Brigidi and Severi maintained that cystic disease of the kidney bore distinct earmarks of tumor formation, and therefore termed it "multilocular adenocystoma." This view was upheld by many other observers, but it may in general be said that proofs of the neoplastic theory of cystic disease of the kidney have been lacking.

The theory which is now generally accepted was first suggested by von Mutach. He believed that cystic disease of the kidney was due to anomalies in the organ resulting in imperfect development. This theory is supported by the fact that other anomalies and malformations are often associated with this condition. According to Moschcowitz there is present a striking association between cystic disease of the kidney and congenital malformations in the genito-urinary system. Among the many other malformations often associated with cystic disease of the kidney the following may be mentioned: hare-lip, cleft palate, meningocele, spina bifida, absence of extremities, or polydactylism, hypospadias, atresia and absence of a ureter, double vagina, absence of bladder, imperforate anus, heart defects.

In about one-fifth of all cases of cystic disease of the kidney cysts in the liver and in other organs are encountered.

Although the great majority of modern writers are of the opinion that cystic disease of the kidney is always due to an error of development, some authors (Heimann, for example) still maintain that no one theory will fit all cases.

Heredity also plays a rôle in the etiology of this condition. Several cases of cystic disease of the kidney have been reported in members of one family. Males are more often affected than females. Most of the cases reported have occurred in adult life. A few cases have been observed in the new-born. Hardly any cases have been reported between the ages of 5 and 15.

Symptoms.—The symptoms of cystic disease of the kidney are dependent on the following: 1. Presence of the tumor masses. 2. Interference with kidney function. 3. Pressure. 4. Presence of malformations. Although in adults the kidney tumors may not reach huge proportions, they are at times enormously enlarged in infants. The enlargement may be unilateral or bilateral. The tumor masses are situated in the flanks, but owing to their progressive increase in size, they may reach from the costal margin to the pelvis, and centrally

to the median line. When large, the masses can be felt in the lumbar region. In the absence of marked intestinal distention the percussion note over the tumors is dull. Their surface is usually somewhat irregular, and their consistency firm. Owing to their small size and their diffusion throughout the kidney tissue, the cysts themselves can only rarely be felt. At times the enlargement of the kidneys is barely perceptible, but in these cases some fulness may be felt in the flanks, a fact of diagnostic importance.

Alteration in kidney function is invariable, but, since the urinary changes are often transient, it has been claimed that a normal urine may exist in this disease. The disturbed kidney function is shown by the presence of albumin, casts, and occasionally by blood in the urine. Although these findings may not be discovered at the first examination, repeated search will reveal them, especially when the disease is moderately well advanced. The phenolsulphonephthalein and other functional tests are also of value in this respect. Due to the accompanying nephritis, there may be, and there often is, increased arterial tension, and, with this, an hypertrophied heart. Where there is very extensive destruction of kidney tissue, the excretory function is so reduced that uremic convulsions and coma may ensue.

Pressure by the tumor is manifested either by the signs of intestinal obstruction or of renal colic. The latter results from the obstruction to the ureters, the former by pressure on the colon as it passes over the kidney. Intestinal obstruction has often been the cause of an immediate operation for its relief. Since polycystic disease of the kidney is in the category of congenital deformities, it is not rare to find other malformations present in this disease; when present they are therefore of some importance in the diagnosis.

Diagnosis.—The diagnosis of polycystic disease of the kidney is rendered extremely difficult at times by the absence of palpable enlargement of the kidneys; when only one organ is enlarged it may be mistaken for a renal neoplasm. The misplaced or greatly enlarged cystic kidneys may be confused with tumor growths of other viscera, the spleen or liver, for example. That the diagnosis is often overlooked is indicated by the frequency with which the condition is first discovered at the autopsy table, or at abdominal operations for other conditions. According to Preitz the following characteristics are diagnostic: 1. Palpable tumor mass. 2. Usually bilateral. 3. Irregular surfaces. 4. Accompanying cysts of the liver. 5. Typical deformity of the abdomen. 6. Diminished kidney function. 7. Uremic attacks. 8. Exploratory puncture. 9. Heredity. To these may be added: 10. Other malformations. 11. Hypertrophy of the heart. 12. Urine that shows the changes of a chronic nephritis.

As to the first of these signs, namely a palpable tumor, a survey of all the case reports will show that a mass was palpable in about 50 per cent. of the cases only, and a bilateral tumor very much more rarely. When only one kidney tumor is palpable, however, a fulness may sometimes be felt in the opposite flank, for in most cases, both kidneys are involved to a greater or less extent.

The surface of the tumor is usually irregular, and at times the tense fluctuating larger cysts can be determined by palpation. Liver cysts are too small to be of any value as a diagnostic sign. The abdominal deformity consists of an enlargement, and is not typical. Diminished kidney function cannot be accepted as a pathognomonic sign, for many patients live through adult life with large polycystic kidneys, and have an apparently normal urinary output. Uremic attacks occur late in the disease only, and are of no value in deciding on the condition. Exploratory puncture is out of the question on account of its danger. It is claimed that heredity is of value in the diagnosis, but in so few cases was a familial history present that not much stress can be laid on this point. The presence of other malformations is of some aid, for in many cases deformities of some kind have existed. They should, therefore, always be looked for. Cardiac hypertrophy is almost always present, the result of the nephritis with its high blood pressure.

Of all the signs, therefore, most stress should be laid on the presence of a tumor either in one or both flanks accompanied by a nephritic urine, and an hypertrophied heart. In infants with these signs, especially if the tumors are bilateral, the presence of polycystic disease of the kidney is almost certain.

Prognosis.—The prognosis of polycystic disease of the kidney varies with the individual case. At times, the disease has progressed so far in intra-uterine life that delivery is interfered with and the infant is born dead. Again, the infant may be born alive, but the tumor masses may be so large as to interfere with the infant's respiration and cause death. Some individuals, on the other hand, present absolutely no symptoms, and live to be 80 or 90 years of age. The prognosis, therefore, depends largely on whether one or both kidneys are affected, and on how much kidney tissue is functionating. The most favorable cases are those in which the chief involvement is confined to one kidney, and the opposite organ shows compensatory hypertrophy. In advanced cases death results suddenly with the symptoms of uremia or cerebral hemorrhage.

Treatment.—Medical treatment is entirely symptomatic. Nephrectomy should never be employed, inasmuch as both kidneys are usually

involved, and death ensues almost invariably. If the tumor masses are very large, and there is much pain and discomfort, multiple puncture of the larger cysts is indicated. This operation has been employed by Kammerer, Curtis, Rovsing, and recently by Lund with very favorable results. The size of the kidney is greatly reduced by this procedure, and much relief is afforded the patient. At times renal function is also much improved.

701 Madison Avenue—The German Hospital.

PROGRESS IN PEDIATRICS

RECENT PROGRESS IN PEDIATRICS

RÉSUMÉ ON THE CIRCULATION *

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THE SIGNIFICANCE OF THE NORMAL ELECTROCARDIOGRAM †

The marked progress which has been made in recent years in the study of the pathology of heart function has been largely due to the introduction of the polygraph and the electrocardiograph, especially the latter. Until very recently, however, the exact significance of the various waves of the ventricular electrocardiogram has not been understood and the clearing up of this difficulty will undoubtedly add greatly to the usefulness of this instrument in the future. Lewis and his collaborators[1, 2, 3, 4] with the aid of the double string galvanometer have recently contributed a large number of new facts to this field. So far, the following things have been determined: The heart beat originates in the head or upper part of the sino-auricular node. From here the excitation wave spreads over the auricles in every direction, following the main muscle bundles, at a uniform speed of about 1,000 mm. per second.[1]

This wave reaches the ventricles after a period of from 0.12 to 0.17 second (in man), most of this time being consumed, according to the experiments of Hering,[5] in the passage of the wave through the node of Tawara. The excitation wave enters the ventricles by way

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† For the convenience of those not familiar with the electrocardiogram, the normal electrocardiogram of an adult with simultaneous venous pulse is shown in Figure 1. This electrocardiogram was taken in Lead II (right arm and left leg), and the sensitivity of the galvanometer was so adjusted that an ordinate of 1 cm. represents an electrical potential of 1 millivolt. The Q wave, as often happens, is not well developed in this electrocardiogram. In taking Lead I the electrodes are attached to the right arm and left arm, and in taking Lead III the left arm and the left leg are the extremities used.

1. Lewis, Meakins, and White: Philosoph. Trans. Roy. Soc. Lond., 1914, Series B, ccv, 375.
2. Lewis, T.: Lectures on the Heart, 1915, New York.
3. Lewis, T.: Proceedings Physiological Society, March 13, 1915. Reported in Jour. Physiol., 1915, xlix, No. 4, p. 20.
4. Lewis, T.: Proceedings Physiological Society, May 15, 1915. Reported in Jour. Physiol., 1915, xlix, No. 5, p. 26.
5. Hering, H. E.: Arch. f. d. ges. Physiol., 1910, cxxxi, 572.

of the His bundle and is very quickly distributed to the endocardial surface of both ventricles by the Purkinje fibers. The speed of the wave along these special structures is very rapid, being approximately 2,000 mm. per second. The excitation wave reaches the epicardial surface of the ventricles by passing out through the ventricular walls in a direction at right angles to the endocardial surface of the muscle at the comparatively slow speed of 400 mm. per second.[2] Since the wave reaches all points on the endocardial surface at about the same time, it will be seen that the time of its appearance at any point on the external surface of the ventricles will depend on the thickness of the muscle at this point, and the excitation wave will appear first where the muscle is thinnest. It is this first spread of the excitation

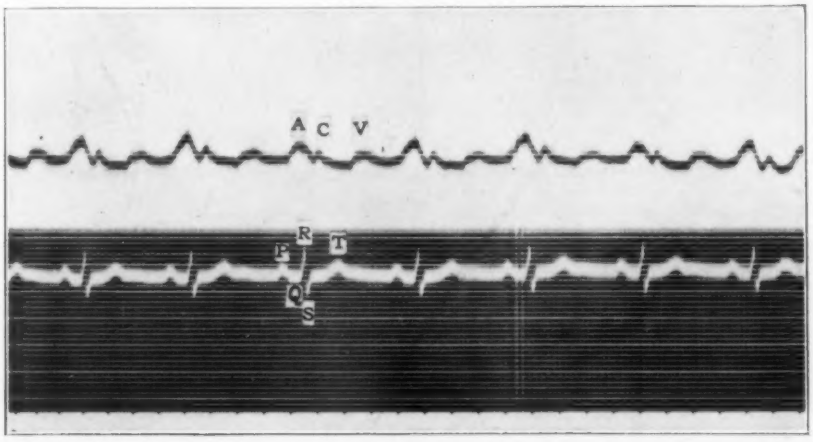

Fig. 1.—Lead II. In this as in the following figures, an ordinate of 1 cm. is equal to 1 millivolt. A normal electrocardiogram with simultaneous venous pulse. The P wave of the electrocardiogram and the *a* wave of the venous pulse represent auricular contraction. All other waves represent ventricular contraction.

wave over the ventricles which is responsible for the QRS group of the electrocardiogram and the configuration of this group of waves therefore depends largely (if we disregard the effect of the position of the heart, the derivation, etc.) on the distribution of the ventricular muscle. It is for this reason that the QRS group is so profoundly modified by the preponderance of the one or the other ventricle.

Lewis[3, 4] has also shown that the ventricular electrocardiogram is a bigram, and that it is formed by the algebraic summation of the right ventricular electrocardiagram (dextrogram) and the left ventricular electrocardiogram (levogram). The dextrogram and the levogram of the monkey, in which animal the heart structure closely approaches that of man, correspond very closely to the clinical curves

which have been regarded as characteristic of left and right bundle-branch block, respectively (Figs. 2 and 3). In other words, the dextrogram is diphasic and the initial deflection is directed downward in Lead I and upward in Lead III, and the levogram is similar except that the direction of the initial deflection in these leads is reversed. These facts indicate that in Lead III Q and S are due to left and R to right ventricular effects (Figs. 2 and 3), while in Lead I the opposite is true. The significance of the T wave is as yet less perfectly understood.

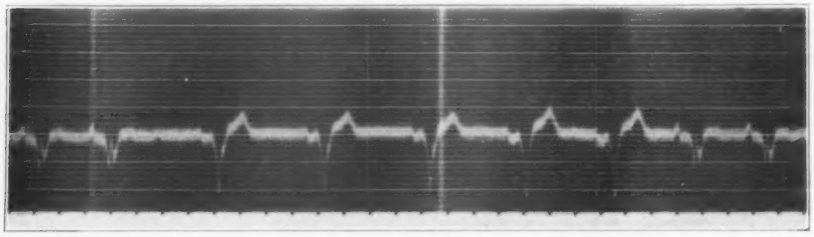

Fig. 2.—Lead III. A gradual transition from ventricular complexes of the normal type to ventricular complexes characteristic of a block in the right branch of the His bundle. The R wave of the normal complex, which is due to right ventricular effects, gradually disappears as the block becomes more marked. An A-V rhythm of Type 1 (see Fig. 4) was present during the branch block.

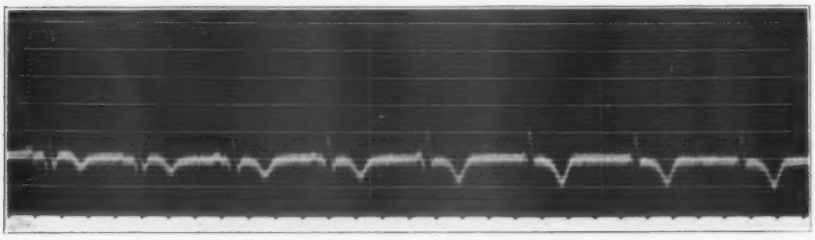

Fig. 3.—Lead III. From the same patient as the previous figure. A gradual transition from ventricular complexes of nearly normal outline to ventricular complexes characteristic of a block in the left branch of the His bundle. The Q and S waves of the normal complex, which are due to left ventricular effects, gradually disappear as the block becomes more marked. An A-V rhythm of Type 2 (see Fig. 5) was present during the branch block.

THE NORMAL ELECTROCARDIOGRAM OF THE CHILD

The normal venous pulse of the child does not differ greatly from that of the adult. A similar statement can not be made, however, in regard to the electrocardiogram. According to Hecht,[6] the electrocardiograms of nurslings are absolutely smaller than those of older

6. Hecht, A. F.: Ergebn. der inn. Med. u. Kinderh., 1913, xi, 324.

children and in addition to this there are other differences which will be discussed in order.

The S Wave.—In nurslings the S wave of the electrocardiogram was found to be unusually prominent by Funaro,[7] by Heubner,[8] and by Funaro and Nicolai.[9] This large S wave became gradually smaller during the first year of life. Hecht[6] examined a large number of children with the electrocardiograph and was able to confirm the observations of these authors. He found that in Lead I the S wave of the electrocardiogram of the new-born infant was on the average three times as large as the R wave. In adults the S wave is relatively only one-tenth as large. The S wave of Lead II was also exaggerated, but less than that of Lead I. In both leads the S wave decreased in size as the child grew older. Hecht believes that the unusual prominence of the S wave in early infancy is not due to the high diaphragm of this period of life, as supposed by other authors[7, 8, 9]; but to some peculiarity of the infant's heart. Lewis[10] has also investigated this subject using all three leads. His results were similar to those obtained by other observers, but he pointed out that the electrocardiograms of the new-born correspond to those obtained in adults with hypertrophy of the right ventricle. He believes that the prominent S waves of Leads I and II during early infancy is due to the preponderance of the right ventricle during this period. According to this observer, the electrocardiogram changes to the adult type between the second and third months of extrauterine life.

The Q Wave.—Hecht[6] found also that the Q wave was more frequently present in the electrocardiogram of the new-born than in that of older children. In his series of cases, this wave never occurred in Lead I, occurred occasionally in Lead II, and was frequently present in Lead III. It seems likely that this peculiarity of the electrocardiogram of the infant is also due to right ventricular preponderance.

The P-R Interval.—Kent[11] has shown that the As-Vs interval in young animals is shorter than in adults and according to Hecht[6] the same is true of man. He found that the P-R interval increases gradually from infancy to puberty. At birth and during the nursing period it averages 0.10 second in duration, during the early years 0.13 second, and at puberty 0.14 second. In adults the normal P-R interval varies from 0.12 to 0.17 second.[12]

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7. Funaro: Riv. di clinica paediat., 1910, viii, No. 6. Quoted by Hecht, Note 6.
8. Heubner: Monatsschr. f. Kinderh., vii, 1. Quoted by Hecht, Note 6.
9. Funaro and Nicolai: Quoted by Hecht, Note 6.
10. Lewis, T.: Clinical Electrocardiography. London, 1913.
11. Kent, A. F. S.: Quoted by Hecht, Note 6.
12. Lewis, T.: Mechanism of the Heart Beat. London, 1910.

THE VAGUS NERVES AND RESPIRATORY ARRHYTHMIA

Effect of the Vagus Nerves upon the Pace-Maker.—The researches of Eyster and Meek[13, 14] and of Lewis and his collaborators[1, 15] have added considerably to our knowledge of the influence of the vagus nerves on the heart. These authors have found that the slowing of the heart which is produced by stimulation of the vagi is accompanied in dogs by a downward displacement of the pacemaker within the sinoauricular node.[1, 14] Occasionally, the displacement of the pacemaker is still more marked and vagus stimulation produces an atrioventricular rhythm.[13, 15] Clinically also, an A-V rhythm may appear as a result of vagus stimulation[16, 17] and it is possible that this sometime occurs in children.[18] It is probable that the appearance of A-V rhythm on stimulation of the vagus nerves is due, in these instances at least, to the fact that, as has been shown by Eyster and Meek,[19] the vagus nerves exert more of an inhibitory effect on the sinus node than on the A-V node. According to these authors the inhibitory effect of the vagi upon the various centers in the system of specialized tissue found in the heart diminishes as we move from the sinus node downward.

The Oculocardiac Reflex.—The oculocardiac reflex in children has been investigated by Gunson.[18] The afferent path of this reflex lies in the fifth cranial nerve, the efferent path in the vagi most often, but occasionally in the sympathetic system. The reflex is considered positive when ocular pressure slows the heart. Gunson's series of cases included fifty cases of diphtheria and twenty-five cases of scarlet fever. The reflex was positive in 92 per cent. of the patients convalescent from these diseases. It was negative in 8 per cent. and was often negative when the heart was rapid during the period of pyrexia. It was also negative in patients with gallop rhythm, cardiac dilatation, hepatic enlargement, and marked arrhythmia—a syndrome which is termed "cardiac paralysis." In some of the cases in which the reflex was positive he observed complete inhibition of the heart for as long as four seconds, reduction of the a-c interval due to A-V rhythm or escape of the ventricles, and complete dissociation of auricles and ventricles. The last was observed in cases of diphtheria only.

Respiratory Irregularity.—Hecht[6] has shown that the respiratory irregularity which is physiologic and practically universal in children,

13. Eyster and Meek: Heart, 1914, v, 227.
14. Meek and Eyster: Am. Jour. Physiol., 1914, xxxiv, 368.
15. Lewis, T.: Heart, 1914, v, 281.
16. Wilson, F. N.: Arch. Int. Med., 1915, xvi, 86.
17. Gallavardin, Dufourt, and Petzetakis: Arch. d. mal. du coeur, 1914, vi, 1.
18. Gunson, E. B.: Brit. Jour. Child. Dis., 1915, xii, 97.
19. Eyster and Meek: Am. Jour. Physiol., 1915, xxxvii, 177.

becomes more marked from birth to puberty; that is, the difference between the shortest and the longest pulse period gradually increases as the heart rate decreases. The dependence of the grade of the arrhythmia on the heart rate can be shown by dividing a group of children of nearly the same age into two classes, those with rapid and those with slow heart rates. It will then be found that the respiratory arrhythmia is more marked in the second than in the first class. The average difference between the shortest and the longest pulse period at various ages, measured in fiftieths of a second, is shown in the following table taken from Hecht's recent monograph:[6]

At birth	3.4	Young children	6.25
Nurslings	2.8	Older children	8.4
Prematurely born	2.5		

ATRIOVENTRICULAR RHYTHM

Atrioventricular rhythm, formerly considered very rare, has been found quite frequently in recent years, often during the course of one of the acute infectious diseases, especially diphtheria. The presence

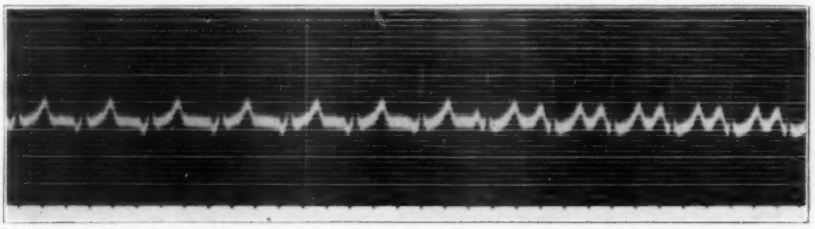

Fig. 4.—Lead II. A transition from an A-V rhythm of Type 1 to the normal rhythm. During the A-V rhythm P is inverted and the As-Vs interval is markedly reduced.

of this rhythm is recognized from polygraphic tracings by a reduction of the a-c interval. The gradual reduction of this interval which is seen when transitions between the normal and the abnormal rhythm are graphically obtained is especially characterisic. In the electrocardiogram, the presence of an atrioventricular rhythm is recognized by the reduction of the P-R interval and the inversion of P in Leads II and III when this wave is not buried in the ventricular complex so that it is not separately distinguishable. There are three types of A-V rhythm, depending on the level within the junctional tissues at which the abnormal rhythm originates. In the first type (Fig. 4) the P-R interval is present, but reduced; in the second type (Fig. 5) the P-R interval is zero, and in the third type (Fig. 6) there is an R-P interval. The last two types can not be distinguished one from the other by polygraphic tracings since the simultaneous contraction of auricles and ventricles which takes place in both types causes a single

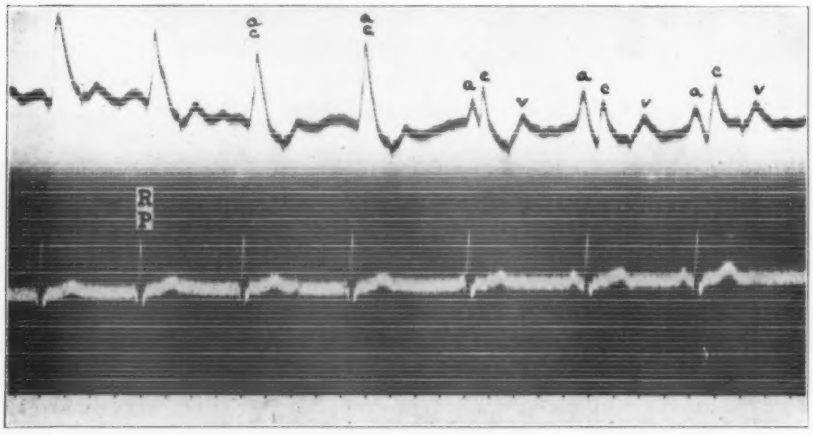

Fig. 5.—Lead II. A transition from an A-V rhythm of Type 2 to the normal rhythm. During the abnormal rhythm the P-R interval is zero and P is not visible, as it is buried in the ventricular complex. The *a* and *c* waves cannot be separately distinguished in the venous pulse during the A-V rhythm. At the end of this rhythm the change in the length of the a-c interval is gradual.

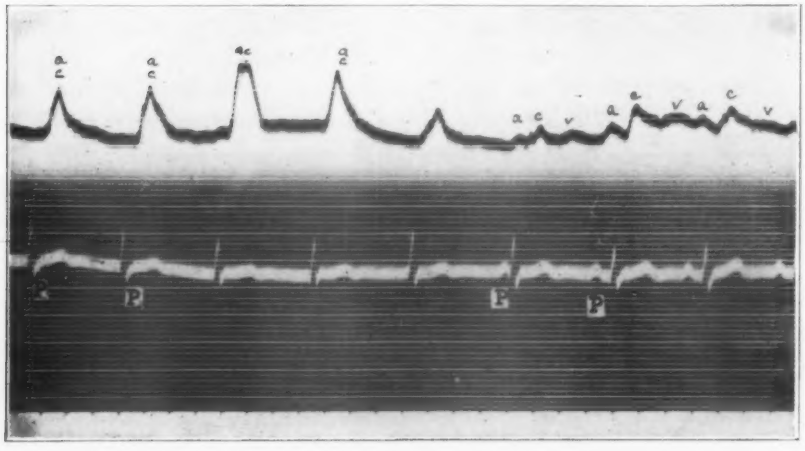

Fig. 6.—Lead II. A transition from A-V rhythm of Type 3 to the normal rhythm. During the abnormal rhythm P falls just after R and is inverted. At the end of the A-V rhythm auricular and ventricular contractions gradually return to their normal time relationship. As long as auricles and ventricles contract simultaneously, there is a large composite wave in the venous pulse, but the auricular and ventricular elements of this wave are not separately distinguishable.

large wave in the venous pulse (Figs. 5 and 6) which is due to the fact that the auricles being unable to force their blood into the ventricles, since the auriculoventricular valves are closed, force it back into the veins. It is impossible to separate the auricular and the ventricular elements in this large wave and so estimate the time relationships of the contractions of auricles and ventricles.

Atrioventricular rhythm has been observed in children suffering from diphtheria by Rohmer,[20] Hume,[21] and others, in cases of typhoid, scarlatina, and rheumatic fever by Belski,[22] and in cases of acute endocarditis by Cowan, Fleming, and Kennedy.[23] Since in most of the above cases only polygraphic tracings were taken, it is impossible to tell what type of A-V rhythm was present but it seems likely to me from an inspection of the tracings published that Type 2 was the most frequent. The exact cause of the appearance of atrioventricular rhythm in such instances is not certain. It seems possible, however, that it is due in some instances to inflammatory lesions of the sinus node which interfere with its function, since in two of Hume's cases which showed this rhythm, inflammatory changes were found in this node at necropsy. In both cases the A-V node and bundle were found to be practically normal. Another possible cause for the appearance of A-V rhythm, however, may be pointed out. I[24] have been able to show that the heart shows an unusual tendency to develop this rhythm during a certain period after the administration of atropin, and possibly other toxic substances may act in a similar manner. Atropin seems to produce this tendency toward A-V rhythm by a selective action on the fibers of the vagi which go to the junctional tissues.

HEART BLOCK IN CHILDREN

Occurrence.—Three types of heart block have been observed in man, sino-auricular block, A-V bundle branch block, and auriculoventricular block. So far as I know, the first two types have not yet been observed in children. Auriculoventricular block, however, is not uncommon in childhood. It has been observed frequently in acute rheumatic fever and in diphtheria, and less often in influenza and other acute infectious diseases. Syphilis, which is a common cause of heart block in adults, seems infrequently or never to produce this condition in children.[6] That heart block may occur in some of the acute infectious diseases without any accompanying structural changes in the A-V bundle has been shown by two fatal cases of diphtheria, one

20. Rohmer, P.: Jahrb. f. Kinderh., 1912, lxxvi, 391.
21. Hume, W. H.: Heart, 1913-14, v, 25.
22. Belski: Ztschr. f. klin. Med., 1909, lxvii, 515.
23. Cowan, Fleming, and Kennedy: Lancet, 1912, i, 277.
24. Wilson, F. N.: As yet unpublished.

reported by Price and MacKenzie[25] and the other by Hume,[21] in which heart block was present although the A-V bundle was negative at necropsy in each case.

Digitalis in large doses may produce heart block in children[6, 26] as well as in adults, especially if the conductivity of the His bundle be somewhat impaired before the drug is given. Hecht[6] reports a case of heart block in a patient, aged 15 years, with hydrocephalus, and thinks it possible that in this instance the block was due to stimulation of the vagus center by the increased intracranial pressure. Atropin was given and produced a ventricular arrhythmia but did not remove the complete A-V dissociation present.

Whipham[26] has recently reported two interesting cases of heart block in children with congenital heart lesions. The first child observed was 2 years and 2 months old. The heart was enlarged to the right and was globular in shape. There was a loud systolic murmur on auscultation. The pulse rate varied from 48 to 80 and the electrocardiograms showed that a 2-1 block was present. The child had a marked polycythemia, 8,400,000 red cells per c.mm. of blood, and a hemoglobin of 110 per cent. The second patient was a girl, aged 12 years, who had had measles but no other illnesses. She complained of precordial pain on exertion. There was no cyanosis. The pulse rate varied from 50 to 60 per minute and the electrocardiograms showed on some occasions complete block, while on other occasions the block was 2-1, 3-2, and mixed. The clinical diagnosis in each case was incomplete ventricular septum.

The Effect of Atropin.—Hecht[6] has reported some interesting observations on the effect of atropin on heart block in children. A 2-1 heart block in a child, aged 3 years, who was suffering from measles complicated by a secondary infection (influenza?) and who had received small doses of digitalis, was completely removed by the injection of atropin (0.0006g). A heart block in a child of like age with diphtheria was, however, not at all affected by this drug. The heart block was transient in the first case while in the second it was still present four months after the first examination.

A third case is still more interesting. The patient was a child, aged 5 years, with measles and influenza. Electrocardiograms showed complete heart block to be present. The idioventricular rate was 47 and the auricular rate 100. The child was given 1 mg. of atropin, which did not remove the block but increased the ventricular rate to 90 and the auricular to 142 per minute. Hecht believes that in this

25. Price and Mackenzie: Heart, 1911-12, iii, 203.
26. Whipham, T. R.: Proc. Royal Soc. Med., Nov. 27, 1914. Reviewed in Brit. Jour. Child. Dis., 1915, xii, 11.

case atropin increased the idioventricular rate by removing the inhibitory effect of the vagi on the ventricular center. So far as I know, a similar result has not been previously obtained by the administration of atropin in cases of complete heart block, and it has been well established that as a rule the idioventricular rhythm in this condition is not under vagus control. It has been suggested that the reason for this is that the lesion which destroys the muscular fibers of the A-V bundle also interrupts the nervous connection between auricles and ventricles.[2] It is also possible that whether or not the vagus nerves have any effect on the idioventricular rhythm depends on the level within the junctional tissues at which this rhythm originates.[27]

Stokes-Adams Attacks.—Another case of heart block is reported by Hecht[6] in a child, aged 9 years. The block appeared after an attack of valvular endocarditis and was complete. The patient had attacks of unconsciousness and fainting spells, which were probably Stokes-Adams attacks. The ventricular rate was 40 and the auricular rate varied from 90 to 103. Hecht pointed out that in this, as in some of his other cases of complete heart block, the interauricular period was always shorter whenever a ventricular contraction fell between the two auricular contractions. The ventricular complexes of the electrocardiogram in this case were abnormal and resembled closely those seen when there is a block in one branch of the His bundle.

PREMATURE BEATS

Although according to Lewis[28] premature beats make up about 35 per cent. of the irregularities encountered in patients between adolescence and old age, they are very uncommonly found before the end of the first decade. When they do occur at this period of life it is usually in the course of some of the acute infectious diseases or in patients with evident cardiac disease. In children, premature beats arising in the auricles are apparently much more common than those arising in the ventricles, while the reverse is true in adults. Gunson[29] examined with the polygraph 120 cases of diphtheria and found auricular extrasystoles in 28 per cent., while ventricular extrasystoles were not observed in any of the cases. In the mild and moderately severe cases the extrasystoles were not associated with other signs of cardiac involvement, and were ignored in treatment. In five severe cases the extrasystoles were very numerous and there were signs of cardiac decompensation with gallop rhythm. Three of these patients

27. Zander, E.: Nordisches med. Arch., 1915, ii, No. 6, Part 2. Reviewed in Zentralbl. f. Herz u. Gefässkrank., July 1, 1915, p. 194.
28. Lewis, T.: Clinical Disorders of the Heart Beat. London, 1913.
29. Gunson, E. B.: Brit. Jour. Child. Dis., 1914, xi, 385.

died. Atrioventricular extrasystoles are rare at all ages. They have been observed in children by Gunson,[29] Lewis and Allen,[30] Hume,[21] and others. Premature beats tend to be abolished by fever or anything which increases the heart rate.

The significance of extrasystoles is still in dispute. Visco[31] observed extrasystoles 48 times in a series of 1,000 observations on healthy and sick children, twice in normal children, 18 times in digestive disturbances and infections, once after the taking of belladonna, 14 times in dyscrasias, 3 times in epilepsy, 10 times in convalescents and patients with diseases of the skeleton. He thought they had very little significance. The experience of Hecht[6] and others, however, does not agree with this conclusion. Extrasystoles are much more serious when they occur before the tenth year and after middle age than they are when they occur during the intervening period of life. They are also more serious when they occur in patients with other signs of cardiac disease than when such signs are absent. Extrasystoles, as such, are of little moment unless they are so numerous as to cause circulatory embarrassment, which is infrequent, and they require no special treatment. They are sometimes, however, the precursors of more serious disorders of the cardiac mechanism and they may also indicate involvement of the myocardium.

AURICULAR TACHYSYSTOLE

Paroxysmal tachycardia of auricular origin and auricular flutter are very similar conditions. We are dealing in each case with very rapid coördinated auricular systoles and in each case these auricular contractions are ectopic in origin; that is, they arise outside the sino-auricular node. In adults the two conditions differ from each other in three particulars. First, in paroxysmal tachycardia the auricular rate is as a rule below, in auricular flutter above, 200 per minute. Second, in paroxysmal tachycardia the ventricular rate is the same as the auricular, while in auricular flutter, probably because of the extremely rapid rate of the auricular contractions, there is usually some heart block, so that the ventricular rate is a simple fraction of the auricular. When the patient first comes under observation the block is most often 2 to 1 so that the ventricles contract only one-half as many times as the auricles. Third, although in each of the two conditions the attacks of abnormal heart mechanism begin and end suddenly, the attacks of auricular flutter are as a rule much more persistent than attacks of paroxysmal tachycardia, their duration being

30. Lewis and Allen: Am. Jour. Med. Sc., 1913, cxlv, 667.
31. Visco: Quoted by Hecht, Note 6.

measured in months or years rather than in hours or days. The administration of digitalis, which is the proper treatment in auricular flutter, after first increasing the heart block, often transforms this condition into auricular fibrillation. Later when this drug has been discontinued the normal heart mechanism may return. Digitalis is not often given in paroxysmal tachycardia because the attacks are usually short and require comparatively little treatment, and the production of fibrillation is inadvisable.

Both auricular flutter and paroxysmal tachycardia have been observed in children, but there is some confusion as to the separation of the two conditions at this period of life. The reason for this is that in children the auricular rate may often exceed 200 per minute without any block being present, and moreover, the attacks of very rapid auricular action so far observed in children have all been of comparatively short duration. We shall not attempt to distinguish between the two conditions, therefore, in this article, but shall refer to both as auricular tachysystole, giving the main features of the heart mechanism in each case mentioned.

Hutchinson and Parkinson[32] report a case in a child aged 2¾ years. The first attack lasted until the twelfth day and was accompanied by edema of the face, the general appearance being similar to that seen in acute nephritis, and by edema of the legs and marked oliguria. There were three subsequent attacks lasting from 12 to 48 hours which were not accompanied by signs of cardiac decompensation other than enlargement of the liver. The heart rate varied from 212 to 245 per minute. One attack stopped when the child vomited and another shortly after defecation. The electrocardiograms taken during the attacks are decidedly abnormal and difficult of interpretation. It seems to me possible from an inspection of the tracings that the paroxysms were of ventricular origin. No premature beats were observed between attacks and the cause of the condition could not be determined. The usual heart rate between paroxysms was 84 to 105 per minute. The authors mention five other cases of "paroxysmal tachycardia" in children reported in the literature.

Kidd[33] has reported a case of "paroxysmal tachycardia" in a child, aged 4½ years. In one attack which lasted five days the heart rate was continuously 240 per minute and there were definite signs of cardiac decompensation. About one year after this attack the patient was again admitted to the hospital with a pulse rate of 150, and marked dulness to the right of the sternum, and enlarged liver. The pulse rate

32. Hutchinson and Parkinson: Brit. Jour. Child. Dis., 1914, xi, 241.
33. Kidd, P.: Proc. Royal Soc. Med., Feb. 24, 1914. Reviewed in Brit. Jour. Child. Dis., 1914, xi, 264.

varied from 80 to 240 and six months later the patient died with severe cyanosis and rapidly developing edema, the heart condition having remained the same in the interim.

Hume[21] has reported a case of "paroxysmal tachycardia" in a child, aged 6, with diphtheria. On the forty-first and fifty-first days of the illness short periods of tachycardia were recorded with the polygraph. The child was vomiting and in a grave, collapsed condition. The author thinks it probable that the attacks originated in the junctional tissues. They did not continue and the patient recovered. In a second case of diphtheria reported by the same author[21] the polygraphic tracings were not convincing but were interpreted as indicating that the auricles were contracting at a rate of 500 per minute while the ventricles were beating only one-fifth as fast. At autopsy a marked myocarditis was found to be present, the auricular muscle showed fatty degeneration, and the ventricles a marked interstitial inflammation with degeneration of the muscle fibers.

Sutherland[34] has recently reported two cases of auricular tachysystole in children with acute rheumatic carditis. The first patient was a girl, aged 8 years. The auricles, as shown by polygraphic tracings, were contracting at a rate of 280 while the ventricles were contracting only one-half as fast. The heart rate after the attack was 105. The second patient was a girl aged 6 years. In one attack the auricles were contracting at a rate of 250, while the ventricular rate was 125. Later an attack was observed in which the auricular rate was 390, the ventricular rate 130. Pulsus alternans was present at this time. Both patients had well marked signs of cardiac decompensation and the second patient died. Sutherland suggests that the presence of any of the following conditions in children indicates that the heart mechanism should be examined by graphic methods: 1. Attacks of cardiac asthma occurring suddenly and without any accompanying variations in the cardiac condition. 2. A triple or galloping or cantering rhythm heard on auscultation. 3. Pericarditis without effusion and with great respiratory distress. 4. Dyspnea, cyanosis, and enlargement of the liver out of proportion to the physical signs of disease of the heart. 5. The presence of pulsus alternans.

From an analysis of the above mentioned cases it will appear that auricular tachysystole in children is often of serious import and is usually accompanied by signs of cardiac decompensation, especially increase in the size of the liver. The symptoms and signs and the seriousness of the condition depend largely on the duration of the attacks and on the underlying causative factor. Lewis reports a case

34. Sutherland, G. A.: Brit. Jour. Child. Dis., 1914, xi, 337.

in an infant in whom the ventricular rate remained at 270 to 290 for several hours without the child apparently suffering any ill effects. According to this author such rates are exceptional and are only tolerated without grave circulatory embarrassment when the heart muscle is sound. High auricular rates have per se little significance if the ventricular rate remains low.

AURICULAR FIBRILLATION IN CHILDREN

While auricular fibrillation is a common clinical condition in adults comprising, according to Lewis'[28] statistics, 40 per cent. of the disorders of the heart beat encountered in an ordinary hospital practice, it is a very rare condition in children. In 1912 Price and Mackenzie[25] reported a questionable case of auricular fibrillation in a child with diphtheria. Complete heart block was also present. More recently three cases of auricular fibrillation during childhood have been recorded. Rheumatic fever was the most probable causative agent in each case.

Sutherland and Coombs[35] observed auricular fibrillation in a child, aged 5 years. The patient became ill suddenly and died after five days. At necropsy the myocardium showed very intense fatty metamorphosis, especially marked in the right auricle, and a very marked inflammatory reaction consisting of proliferative changes and infiltration with endothelial cells. The vascular reaction was marked and there was thrombosis of many of the fairly large vessels. The diagnosis made from the character of the illness and the autopsy findings was acute rheumatic carditis. Polygraphic tracings were published and there can be little doubt of the presence of auricular fibrillation, although electrocardiograms were not taken.

Ehrenreich[36] reports a case of auricular fibrillation in a child, aged 11 years. There was an indefinite history of rheumatism with a history of frequent attacks of cardiac decompensation since the age of 9. Examination showed marked dilatation of the heart, a double mitral murmur, and accentuation of the pulmonic second sound. Auricular fibrillation appeared under digitalis treatment during an attack of cardiac decompensation. Both polygraphic and electrocardiographic tracings were obtained, but these are not published.

A third case of auricular fibrillation was reported by Nadel.[37] The patient was a boy of 11 years of age who had had repeated attacks of rheumatic fever and several periods of broken compensation which

35. Sutherland and Coombs: Heart, 1913-14, v, 15.
36. Ehrenreich, S. G.: New York Med. Jour., 1914, xcix, 269.
37. Nadel, V.: Mitteil. d. ges. f. inn. Med. u. Kinderh., Wien., 1914, xii, 210. Reviewed in Ztschr. f. Kinderh., 1914, viii, 88.

always reacted to treatment. The usual cardiac mechanism was normal except that the electrocardiograms showed an unusually large P summit and a P-R interval of 0.2 second, indicating hypertrophy of the auricular muscle and a slight degree of A-V heart block. Under digitalis treatment for cardiac decompensation, a 2-1 heart block developed and a bigeminy of the extrasystolic type also appeared. Later there was complete heart block with auricular fibrillation, and finally the block became less marked so that the ventricles responded irregularly to the fibrillating auricles. Electrocardiograms taken at this time showed that ventricular extrasystoles were frequent.

In conclusion we may say, therefore, that auricular fibrillation in children is a rare but grave disorder. The treatment is the same as for auricular fibrillation in the adult.

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